University of Alberta

The Prevention of Term Large for Gestational Age Births in Northern and Central Alberta: Identifying Modifiable Risk Factors and Their Public Health Importance

by

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A thesis submitted to the Faculty of Graduate Studies and Research
in partial fulfillment of the requirements for the degree of
Master of Nursing

Faculty of Nursing

Edmonton, Alberta

Spring 2006

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Your file Votre référence
ISBN: 0-494-13771-1
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ISBN: 0-494-13771-1

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Dedication

In loving memory of my parents, David and Sylvia Jaipaul

Abstract

To determine modifiable and non-modifiable risk factors for term large for gestational age (LGA) births in Northern and Central Alberta and their public health importance, a retrospective cohort study of n = 115,198 singleton live births (1996-2003) was conducted using data from a provincial perinatal database. After adjusting for potential confounders using multiple logistic regression analysis, predictors were maternal age 17 years or younger, height 152 cm or taller, prepregnancy weight 91 kg or greater, non-smoking, pre-existing diabetes, gestational diabetes, multiparity, previous LGA birth, hydramnios, and pregnancy-induced hypertension. The strongest modifiable predictor was prepregnancy weight 91 kg or greater, which increased the odds 2.5-fold. The population-attributable risk percentage for prepregnancy weight 91 kg or greater was 10%. Prevention strategies aimed at normalizing prepregnancy weight are essential. Further research and future risk modeling that includes previously identified predictors are also necessary to extend our understanding of the etiology of LGA births.

Acknowledgements

I wish to express sincere gratitude to my thesis supervisor, Dr. Christine Newburn-Cook, for her assistance in preparing my thesis for publication. She is most responsible for helping me to complete the writing of this thesis as well as the research behind it. She showed me how to express my ideas with precision in an academic style and kept me focused on conducting my research. She was keen to discuss ideas and ask challenging questions to help me to anticipate and resolve problems (philosophical, analytical, or computational). Without her guidance, this thesis would have been less comprehensive.

I would like to thank the other members of my thesis committee as well, Dr. Nestor Demianczuk and Dr. Beverley O'Brien, for their assistance, thoughtfulness, and consideration in guiding my studies. Their insightful comments, stimulating discussions, and overall critical review of my work were invaluable. In addition, I am grateful to the Northern and Central Alberta Perinatal Outreach Program for granting me access to the perinatal data required for this study.

I also deeply appreciate the support of my director, Anita Hanrahan, for her genuine interest and constant encouragement in helping me to complete my studies while I worked full-time. She had confidence in me and was always available to listen, give advice, and gently remind me of the need for balance and persistence in accomplishing my goals. She has truly been a mentor and a friend.

I also owe a debt of gratitude to my other friends and colleagues, each of whom contributed whatever support was necessary to help me through my studies.

Finally, thank you to my family for their unconditional love, support, and encouragement, and for helping me to balance industry and satisfaction. To my parents for instilling in me a love of learning; to my siblings for believing in me; to my husband, Manoj, for his unending patience and good humor; and to our son, Joel, for his unique thoughtfulness and loving spirit. I could not have done this without you. I love you all very much.

"If the shoe fits, wear it." (Proverb)

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CHAPTER 1:

INTRODUCTION

Statement of Problem

Birth weight is an important determinant of population health. It is a measure of the availability of good antenatal care, good living conditions, the general health of the pregnant woman and fetus, and how well the pregnancy has progressed. Moreover, birth weight is the single most important predictor of infant survival and morbidity (Alberta Health and Wellness, 1999; Dyck & Tan, 1995; McCormick, 1985; World Health Organization, 1996).

Infant birth weight is receiving increased attention vis-à-vis research into the fetal origins of adult disease (Barker, 1992). Study findings suggest that the size of an infant at birth has an effect on health status throughout the life course. Researchers have reported that intrauterine conditions that result in high birth weight (also referred to as *fetal* or *neonatal macrosomia*, or *large for gestational age*) or preterm birth or intrauterine growth restrictions that result in low birth weight have long-term health implications. High birth weight consequences include hypertension, ischaemic heart disease in adults, certain cancers in childhood, breast and prostate cancer in adults, and non-insulin-dependent (type II) diabetes (Michels et al., 1996; Pettitt & Knowler, 1998; Power, 1994; Tibblin, Eriksson, Cnattingius, & Ekborn, 1995; Yeazel et al., 1998). However, the number of studies that have examined the impact of excessive fetal growth on health and the development of chronic conditions in adulthood is limited.

Studies in which the impact of birth weight on neonatal and infant mortality, as well as infant, childhood, adolescent, and adult morbidity, has been examined were focused primarily on infants born preterm (< 37 weeks' gestational age) and low birth weight infants (weighing < 2,500 g at birth). However, at the other extreme of the birth weight continuum is the large (excessively overgrown) or macrosomic baby with a birth weight ≥ 4,000 g at birth, or > 90th percentile for weight adjusted for gestational age. These latter infants are also referred to as large for gestational age (LGA). Existing studies on these infants have focused primarily on obstetrical problems that could increase the risk of maternal morbidity, as well as infant morbidity and mortality. However, more studies that are aimed at examining risk factor epidemiology need to be conducted in different populations. The identification of predictive factors for macrosomia or LGA births—in particular, modifiable determinants—could lead to the development and implementation of population-based prevention programs.

The macrosomic (≥ 4,000 g) or LGA neonate (> 90th percentile) has not received the same focused inquiry as has the preterm, growth-restricted fetus, despite the fact that the term mean birth weight and high birth weight rates have risen steadily in several developed countries (Ananth & Wen, 2002; Kramer et al., 1998; Rooth, 2003; Surkan, Hsieh, Johansson, Dickman, & Cnattingius, 2004). Fetal macrosomia or LGA birth is clinically important. It is associated with higher rates of perinatal mortality and morbidity and with obstetrical complications that increase maternal morbidity (Berard et al., 1998; Boyd, Usher, & McLean, 1983; Stotland, Caughey, Breed, & Escobar, 2004). Among these adverse outcomes are increased risks of labor abnormalities, instrument and cesarean delivery, postpartum hemorrhage, and traumatic injuries during delivery (Boulet, Alexander, Salihu, & Pass, 2003; Jolly, Sebire, Harris, Regan, & Robinson, 2003).

Since the 1970s both the average birth weight and the incidence of macrosomic or LGA deliveries have risen steadily in many countries, including the United States of America (USA), Canada, the United Kingdom (UK), Norway, and Sweden (Ananth & Wen, 2002; Kramer et al., 1998; Martin, Hamilton, Ventura, Menacker, & Park, 2002; Meeuwisse & Olausson, 1998; Rooth, 2003; Surkan et al., 2004). Because these trends occurred simultaneously with an increase in birth rates, several researchers have suggested that the observed increase in birth weight is the result of an overall increase in fetal growth (i.e., birth weight for gestational age; Ananth & Wen; Kramer et al., 1998; Kramer et al., 2001; Surkan et al.).

Neonatal macrosomia or LGA births are increasingly common. The overall incidence of neonates with birth weights > 4,000 g is estimated across different studies to be between 6.5% and 8.2% (Ferber, 2000). Furthermore, the incidence of birth weight ≥ 4,500 g ranges from 0.8% to 1.5% of the population, and 0.07% to 0.4% of infants weigh ≥ 5,000 g at birth (Alsunnari et al., 2005).

Using country-specific vital statistics data, Rooth (2003) examined and compared increases in mean birth weight and the percentage of newborn infants who weighed ≥ 4,000 g in several European cities and countries including Sweden, Norway, Hessen (Germany), London, Scotland, Zurich, Austria, and Hungary. He reported the trends over a 20-year period between 1978 and 1998. Rooth found that in European countries, birth weight increased on average between 45 and 95 g. With the exception of Finland and Austria, where no increases were observed, the percentage of infants weighing ≥ 4,000 g at birth increased in Sweden (22% to 25%), Denmark (10% to 18%), Germany (7% to 12%), London (7% to 12%), and Zurich (7% to 9%) in the same time period.

Similar increases have been reported in Canada and the USA. Ananth and Wen (2002) determined trends in fetal growth among singleton live births in both Canada and the USA between 1985-1986 and 1997-1998. They specifically examined the mean birth weight and the rates of preterm and term LGA (T-LGA) births and found that the term mean birth weight increased in both countries: an increase of 36 g among Canadian infants and of 8 g and 27 g in White and Black American infants, respectively. Furthermore, T-LGA births increased in the USA (5% among White infants and 9% among Black infants) and by 24% in Canada. Over the same period, preterm LGA births fell by 13% in White American infants, 25% in Black infants, and 14% in Canadian infants. Two other recent studies have also shown temporal increases in the proportion of LGA births in Canada during different time periods and using different databases (Kramer et al., 2002; Wen et al., 2003).

Martin et al. (2002) reported that approximately 10% of USA infants have a birth weight ≥ 4,000 g, and 1.5% weigh at least 4,500 g. In Canada, 12% of infants are LGA (Wen, 2003). Among Canadian Aboriginal populations, the incidence of macrosomia is higher than the national average and is estimated to be between 16% and 36% (Armstrong, Robinson, & Gray-Donald, 1998; Dyck & Tan, 1995; Munroe, Shah, Badgley, & Bain, 1984; Rodrigues, Robinson, Kramer, & Gray-Donald, 2000; Thomson, 1990). Within the province of Alberta, LGA birth rates have also increased steadily from 9.7% in 1988 to 12.1% of live births in 2002 (Alberta Health and Wellness, 2004).

Increasing rates of macrosomic (≥ 4,000 g) or LGA births (> 90th percentile) combined with the increasing prevalence of obesity and type II diabetes mellitus in developed countries (Mokdad et al., 2000) have reinforced the current need to focus our research attention on the epidemiology of high birth weight deliveries. It is necessary to continue to examine secular trends in neonatal macrosomia or LGA births and to identify the potential determinants (exposures and risk factors) associated with these trends. Appropriate identification of predictive factors for macrosomia or LGA births, specifically modifiable exposures and risk factors, could lead to targeted interventions to promote the health of the pregnant mother and her fetus.

There is no universally accepted definition of fetal or neonatal macrosomia. Macrosomia is a rather imprecise term used to describe a very large neonate (Haram, Pirhonen, & Bergsjø, 2002). The term implies excessive fetal growth beyond a specific weight. In the current medical literature, macrosomia has been defined arbitrarily by using either crude (absolute) birth weight (i.e., a birth weight ≥ 4,000 g, ≥ 4,500 g, or ≥ 5,000 g) or centile (relative) birth weight (i.e., birth weight > 90th percentile adjusted for gestational age and gender, referred to as *LGA*; Ananth & Wen, 2002; Boulet et al., 2003; Jolly et al., 2003; Lipscomb, Gregory, & Shaw, 1995; Oral et al., 2001; Stotland et al., 2004). Researchers' use of different definitions makes it difficult to conduct direct comparisons across studies. Moreover, these differences may be responsible for inconsistencies in the medical literature regarding the strength of the association between the risk factors identified as relevant and the occurrence of a macrosomic birth (Boulet et al.).

Regardless of the criteria used to classify births as high birth weight, macrosomic, or LGA, there is an increased risk for shoulder dystocia (Berard et al., 1998; Gregory, Henry, Ramicone, Chan, & Platt, 1998; Jolly et al., 2003; Mulik, Kiran, Bethal, & Bhal, 2002; Orskou, Kesmodel, Henriksen, & Secher, 2001; Raio et al., 2003; Stotland et al., 2004), brachial or facial nerve injuries (Boyd et al., 1983; Oral et al., 2001; Orskou et al.; Raio et al.; Surkan et al., 2004), skeletal injuries including clavicular or humerus fractures (Bergmann et al., 2003; Raio et al.; Surkan et al.), birth asphyxia (Gregory et al., 1998; Oral et al.), and neonatal hypoglycemia (Schaefer-Graf et al., 2002). When associated with maternal diabetes mellitus, high birth weight infants are at increased risk for stillbirth (Mondestin, Ananth, Smulian, & Vintzileos, 2002). Researchers have also shown that the rates of neurological deficits and perinatal deaths increase as the weight of the infant exceeds 4,000 g (Axelsson, 1990; Bryant, Leonardi, Landwehr, & Bottoms, 1998; Spellacy, Miller, Winegar, & Peterson, 1985).

Maternal complications are often associated with cephalopelvic disproportion (American College of Obstetricians & Gynecologists, 2000; Boulet et al., 2003). For mothers, the delivery of a macrosomic or LGA infant is associated with a prolonged or obstructed labor (Dor, Mosberg, Stern, Jagani, & Schulman, 1984; Jolly et al., 2003; Mocanu, Greene, Byrne, & Turner, 2000; Mulik et al., 2002; Stotland et al., 2004), genital tract injury including third- and fourth-degree perineal tears, anal sphincter rupture, and pudendal nerve damage (Berard et al., 1998; Gregory et al., 1998; Jolly et al.; Oral et al., 2001; Orskou et al., 2001; Raio et al., 2003; Stotland et al.), instrument and caesarean section deliveries (American College of Obstetricians & Gynecologists; Bergmann et al., 2003; Boyd et al., 1983; Gregory et al.; Jolly et al.; Mocanu et al.; Oral et al.; Spellacy et al., 1985; Stotland et al., 2004), and postpartum hemorrhage (Gregory et al. 1998; Jolly et al. 2003; Mulik et al., 2002; Stotland et al.). Macrosomic deliveries are also associated with prolonged hospital stays regardless of the mode of delivery (Stotland et al.). Given their increasing frequency and their association with maternal and newborn complications, high birth weight deliveries impose a financial burden on the health care system in a time of significant health care reform (Mulik et al.; Stotland et al.).

Some researchers have suggested that intrauterine conditions that result in fetal overgrowth may alter fetal development and organ maturation. These changes may persist postnatally and have possible long-term metabolic consequences (Aerts & Van Assche, 2003). Silverman et al. (1991) demonstrated the impact of maternal metabolic alteration on the neurophysiological status of infants at birth, as well as its association with intellectual development in childhood. Compared with appropriate for gestational age infants, babies who are born LGA and whose mothers are diabetic and/or obese are at an increased risk of developing metabolic syndrome (obesity, hypertension, dyslipidemia, and glucose intolerance; Boney, Verma, Tucker, & Vohr, 2005). In addition, high birth weight infants associated with maternal diabetes mellitus may develop obesity and type II diabetes mellitus at an early age (Pettitt & Knowler, 1998).

The effects of fetal macrosomia may also have other adverse health implications beyond infancy and into adulthood. Excessive fetal growth has been associated with childhood cancers (Yeazel et al., 1998), breast cancer (Michels et al., 1996) and prostate cancer (Tibblin et al., 1995) in adults, and obesity (Dietz, 2004; Whitaker & Dietz, 1998). There is current speculation that the increased prevalence of high birth weight infants has contributed to overweight and obesity arising from affluent living conditions (Bergmann et al., 2003). Considering global trends towards increased rates of obesity in children and adolescents as well as type II diabetes mellitus, rising LGA birth rates could pose an even more serious problem in the future (Surkan et al., 2004).

Overall, few studies were found in which the epidemiology of high birth weight deliveries was examined, and the majority of these investigations have been conducted in Europe (Bergmann et al., 2003; Jolly et al., 2003; Orskou, Henriksen, Kesmodel, & Secher, 2003; Surkan et al., 2004) and the USA (Boulet et al., 2003; Stotland et al., 2004). There are some Canadian studies and with few exceptions (Kramer et al., 2002; Okun, Verma, Mitchell, & Flowerdew, 1997), the focus of these studies has been high birth weight among Aboriginal populations in Ontario, Saskatchewan, and British Columbia (Armstrong et al., 1998; Dyck & Tan, 1995; Munroe et al., 1984; Rodrigues et al., 2000; Thomson, 1990). Moreover, in previous studies the significant impact of gestational age on fetal growth was not always considered. Instead of correcting birth weight for gestational age and gender to identify LGA births, high birth weight deliveries were often defined using crude or absolute birth weight cutoffs (e.g., ≥ 4,000 g). Jolly et al. recommended that centile or relative birth weight controlled for gestation may be more appropriate in investigating fetal growth or outcomes where gestational age has a significant confounding effect.

Studies that focused specifically on LGA births were generally limited in number, and current studies are required to determine existing trends and to examine population-specific risk factors (both modifiable and non-modifiable). The previous studies were often criticized for inadequate control of potential covariates such as parity (Mocanu et al., 2000) in determining the independent effects of relevant risk factors. Existing study findings are also limited because investigators have not focused on the identification of modifiable risk factors and the determination of their public health importance; that is, on consideration of the prevalence of the risk factors in a particular population and the magnitude of risk associated with it. Primary prevention of LGA births and associated morbidity requires greater understanding of the epidemiology of LGA births in specific populations. Identifying risk factors can help in planning programs aimed at reducing their prevalence to promote maternal and newborn health. Investigators must focus on determining predictive factors (both modifiable and non-modifiable), and the studies must be population based, have adequate power, and control for potential confounders. Successful population-based prevention strategies require the identification of modifiable risk factors that are significant from a public health perspective.

Purpose of the Study

The purpose of this study was to identify both modifiable and non-modifiable risk factors that increase a woman's chances of giving birth to a term infant that is LGA (T-LGA) in Northern and Central Alberta. This information could then be used to determine where and to what extent the prevention of T-LGA births is possible.

Study Objectives

The following objectives were addressed in this study: (a) to estimate T-LGA birth rates in Northern and Central Alberta from 1996 to 2003 and to determine whether these rates have changed over time; (b) to identify the modifiable and non-modifiable risk factors that increase the chances of T-LGA births to women who reside in Northern and Central Alberta (e.g., maternal age, genetic and constitutional factors, pre-existing maternal morbidity, problems during pregnancy, and lifestyle factors); (c) to quantify the relative contribution of these risk factors to the incidence of T-LGA births while simultaneously controlling for other risk factors; and (d) to determine the public health importance of significant modifiable risk factors that could be targeted in population-based prevention programs and interventions aimed at risk reduction and health promotion in pregnant women.

To address these objectives, a population-based retrospective cohort study was used to examine a large series of singleton live-born pregnancies using a well-validated perinatal database. Information on gestational age, birth weight, and infant gender were used to calculate birth weight for gestational age. Infants delivered at 37 to 40 weeks' and six days completed gestation with a birth weight > 90th percentile corrected for gestational age and infant gender were classified as T-LGA births (Kramer et al., 2001). The reference group was comprised of term infants (37 to 40 weeks' and six days completed gestation) with birth weight appropriate for gestational age (T-AGA) between the 10th and 90th percentiles.

Significance of the Study

An epidemiologic and a population health framework were used to guide the development and implementation of this study. These approaches are complementary; both are used to identify the determinants of health and illness from a population perspective and, ultimately, to control or prevent the problem. The focus of the proposed study was women of childbearing age and the identification of maternal and newborn factors that increased the risk of delivering an LGA infant.

Brunt and Shields (2000) noted that epidemiological methods are becoming progressively more important to health professionals, including nurses, as a result of shifting health care priorities that have changed the focus from illness treatment to illness prevention. Understanding the determinants of health and illness is important for primary prevention. However, the role of nurses in identifying determinants of health is still evolving. Nurses have yet to become principally involved in conducting etiological studies. Butterfield (2002) noted that "with a few exceptions, nursing has not been active in efforts to understand the etiology of disease" (p. 33). In her estimation, nurses have an important role in advancing *upstream thinking* through research in which the determinants of diseases that affect their clients are addressed.

The focus of this study was on the identification and quantification of modifiable and non-modifiable risk factors for T-LGA births in a geographically defined population. The identification of modifiable risk factors can be used to develop interventions and/or prevention programs that will decrease risk factor prevalence. The earlier in the causal stream that preventive action is taken, the greater the potential for population health gains (Health Canada, 2002).

An understanding of the etiology of T-LGA births is necessary to persuade health care decision makers and policy planners to allocate limited financial resources to population-based prevention programs. Knowledge of non-modifiable risk factors is also useful in secondary and tertiary prevention efforts (i.e., surveillance, identification of problems, and prompt medical management) to minimize the maternal and infant complications associated with T-LGA births. In addition, study findings may be used in obstetrical practice to screen women at risk for delivering a macrosomic or LGA infant. The risk factors and their associated risk (i.e., the magnitude of the associated odds ratio [OR]) could be incorporated into an antepartum risk scoring system to assess maternal risk for delivering a T-LGA infant in Northern and Central Alberta. The study findings also provide baseline data for possible integration of additional risk factors as identified in other studies that are not currently included in the administrative perinatal database used in Northern and Central Alberta.

Nurses are adept at advocating for risk reduction and health promotion strategies; they continually cultivate reciprocal relationships between individuals, families, and other health care partners to facilitate positive health outcomes (Reutter, 2001). The findings reported in this study will increase the understanding of modifiable and non-modifiable risk factors for T-LGA births and enable nurses to better promote primary prevention strategies or implement secondary measures that alleviate or modify these risks. Such action is important to minimize unfavorable health outcomes and promote optimal birth outcomes, from pre-conception through the postnatal period and beyond.

CHAPTER 2:

LITERATURE REVIEW

The focus of the literature review was on two content areas regarding high birth weight (i.e., neonatal macrosomia [≥ 4,000 g] or LGA [> 90th percentile]). These were (a) the diversity in how researchers have arbitrarily defined high birth weight, and the issues arising from these different definitions (e.g., the variation in the quantification of the effects of different risk factors across studies); and (b) risk-factor epidemiology. This includes a discussion of different maternal and newborn factors, as well as clinical or pregnancy characteristics that have been identified in the medical literature as being associated with macrosomic or LGA births, and their relative impact on birth weight for gestational age.

The literature review was conducted using MEDLINE (1996-2005), CINAHL (1996-2005), EMBASE (1996-2004), HealthSTAR (1996-2004), and the Cochrane database. Articles were retrieved using the following MeSH headings and keywords: *macrosomia*, *high birth weight*, *large for gestational age*, *perinatal trauma*, *shoulder dystocia*, *birth trauma*, *fetal asphyxia*, and *brachial plexus*. In addition, the key words *maternal complications*, *fetal complications*, *mortality*, and *morbidity* were combined with *macrosomia*, *high birth weight*, and *large for gestational age*. Seven studies were retrieved and included in the literature review, and the results of these studies are summarized in Table 1.

Table 1

Characteristics and Results of the Studies Included in the Literature Review

Bergmann, R., Richter, R., Bergmann, K., Plagemann, A., Brauer, M., & Dudenhausen, J. W. (2003). ***Secular trends in neonatal macrosomia in Berlin: Influences of potential determinants.***

Study setting & sample	Purpose	Results	Conclusions
Germany *N* = 206,308 singleton pregnancies from hospital deliveries collated by the Berlin Medical Board between 1993-1999. A population-based study.	To examine secular trends in the prevalence of neonatal macrosomia (≥ 4,000 g) and describe how changes in the potential determinants have affected trends in neonatal macrosomia and short-term outcomes. **Method:** a population-based retrospective cohort study. Data recorded annually, either electronically or on data sheets. Risk factors included: maternal age, prepregnancy body mass index (BMI), height, German nationality, pregnancy weight gain, parity, smoking status, diabetes mellitus, gestational age, and infant gender. Outcome Variable: delivery of a high birth weight baby (defined as a birth weight ≥ 4,000 g). Control group defined as infants with birth weight 2,500 g to 4,000 g. Adequate control of potential covariates by multivariate logistic regression.	**(OR; 95% CI):** Age ≥ 30 years: OR = 1.10; CI 1.06, 1.14 Genetic/ constitutional: Height ≥ 165 cm: OR = 1.94; CI 1.87, 2.01 Prepregnancy BMI 20-26 kg/m^2: OR = 1.92; CI 1.81, 2.03 Prepregnancy BMI > 26 kg/m^2 : OR = 4.01; CI 3.77, 4.26 Pregnancy weight gain 10-16 kg: OR = 1.85; CI 1.77, 1.93 Pregnancy weight gain > 16 kg: OR = 3.37, CI 3.22, 3.53 German nationality: OR 1.06; CI 1.02, 1.11 Lifestyle: Non-smoker: OR = 2.03, CI 1.93, 2.14 Obstetric history: Multiparity: OR = 1.98, CI 1.91, 2.05 Medical conditions during pregnancy: Diabetes mellitus: OR = 1.85, CI 1.69, 2.04 Infant characteristics: Gestational age > 42 weeks: OR = 2.56, CI 2.39, 2.75 Male infant gender: OR = 1.88; CI 1.82, 1.95	Increased risk of giving birth to an infant weighing ≥ 4,000 g for women with older maternal age, increasing maternal height, high prepregnancy BMI, high pregnancy weight gain, multiparity, non-smoking, diabetes, high gestational age, and male infant gender. Increasing high birth weight rates explained by changes in risk factor prevalence over time.

(table continues)

Jolly, M., Sebire, N., Harris, J., Regan, L., & Robinson, S. (2003). ***Risk factors for macrosomia and its clinical consequences: A study of 350,311 pregnancies.***

Study setting & sample	Purpose	Results	Conclusions
United Kingdom *N* = 350,311 completed singleton pregnancies in London between 1988-1997. A population-based study.	To identify demographic risk factors f. . .or either birth weight > 4,000 g or > 90th percentile, test the hypothesis that both absolute birth weight and centile birth weight are associated with increased risk of adverse outcomes, and to quantify the obstetric risks. **Method:** a population-based retrospective cohort study. Data derived from St. Mary's Maternity Information System clinical database which records information from state-funded National Health Service hospitals with the North West Thames Region. Risk factors included: age, ethnic origin, body mass index (BMI), parity, smoking, pre-existing hypertension, diabetes mellitus, and pre-eclampsia. Outcome Variables: delivery of a high birth weight baby defined as a birth weight > 4,000 g or > 90th percentile. Control groups included infants with birth weight 2,500 g to 4,000 g and 10th-90th percentile, respectively. Adequate control of potential covariates by multivariate logistic regression.	**(OR; 99% CI):** **Birth weight > 4,000g** Age: 35-40 years: OR = 1.05; CI 1.01, 1.10 Genetic & Constitutional Factors: BMI > 25-30 (kg/m^2): OR = 1.54; CI 1.48, 1.60 BMI > 30 (kg/m^2): OR = 1.97; CI 1.88, 2.06 Lifestyle: Smoking: OR = 0.47; CI 0.45, 0.49 Pre-existing medical diseases: Diabetes mellitus: OR = 1.81; CI 1.50, 2.19 Obstetric history: Parity = 2-4: OR = 1.60; CI 1.55, 1.65 Parity ≥ 4: OR = 1.92; CI 1.76, 2.09 Medical conditions during pregnancy: Gestational diabetes mellitus: OR = 1.57; CI 1.40, 1.77	Increased risk of giving birth to an infant weighing > 4,000 g and > 90th percentile for women with older maternal age, multiparity, high prepregnancy BMI, and diabetes mellitus. Pre-existing diabetes was the greatest risk factor for birth weight > 90th percentile, whereas maternal BMI > 30 and parity > 4 were the strongest risk factors for birth weight > 4,000 g. Macrosomia defined by crude birth weight is a better predictor of morbidity, whereas macrosomia defined by centile birth weight is more appropriate when investigating the underlying metabolic causes and outcomes in which gestational age has a significant effect.

(table continues)

Jolly, M., Sebire, N., Harris, J., Regan, L., & Robinson, S. (2003). ***Risk factors for macrosomia and its clinical consequences: A study of 350,311 pregnancies.***

Study setting & sample	Purpose	Results	Conclusions
		(continued) (OR; 99% CI): Birth weight > 90th percentile Age: < 18 years: OR = 1.19; CI 1.01, 1.40 35-40 years: OR = 1.14; CI 1.08, 1.19 > 40 years: OR = 1.22: CI 1.11, 1.35 Genetic & Constitutional Factors: BMI > 25-30 (kg/m^2): OR = 1.56; CI 1.50, 1.62 BMI > 30 (kg/m^2): OR = 2.08; CI 1.99, 2.17 Lifestyle: Smoker: OR = 0.54; CI 0.52, 0.57 Pre-existing medical diseases: Diabetes mellitus: OR = 6.97; CI 5.96, 8.16 Obstetric history: Parity = 2-4: OR = 1.76; CI 1.70, 1.82 Parity > 4: OR = 2.20; CI 2.02, 2.40 Medical conditions during pregnancy: Gestational diabetes mellitus: OR = 2.77; CI 2.51, 3.07	

(table continues)

Rodrigues, S., Robinson, E., Kramer, M., & Gray-Donald, K. (2000). ***High rates of infant macrosomia: A comparison of a Canadian Native and a non-Native population.***

Study setting & sample	Purpose	Results	Conclusions
Canada N = 385 singleton live births ≥ 37 weeks' gestation to Cree women of James Bay (January 1995-June 1997) and n = 5,644 non-native Caucasian Canadian women (January 1990-March 31, 1996), who did not have a low BMI (< 1.8 kg/m^2) or pre-gestational diabetes, and were not on glucocorticoid therapy. A population-based study.	To examine independent risk factors for infant macrosomia among the Cree, compare them to non-Natives, and determine if ethnic differences persist after adjusting for differences in risk factors. **Method:** a population-based retrospective cohort study. Data for Cree births abstracted from nutrition intervention study, and the Government of Quebec official declaration of births and the Cree Board of Health and Social Services of James Bay birth registry. Data for non-Native Caucasian Canadian pregnancies were extracted from the McGill Obstetrics and Neonatal Database (MOND), which is a computerized database of births at the Royal Victoria Hospital in Montreal. Risk factors included: maternal age, parity, pregravid weight, height, weight gain, gestational age at delivery, smoking status, and gestational diabetes mellitus. Outcome Variable: delivery of a high birth weight baby (defined as a birth weight > 90th percentile). Control group consisted of non-Native Canadian women who delivered a high birth weight baby > 90th percentile. Adequate control of potential covariates by multivariate logistic regression.	**Cree births (OR; 95% CI)** Genetic & Constitutional Factors: Pregravid weight (per 5 kg): OR = 1.15; CI 1.07, 1.23 Height (per 5 cm increase): OR = 1.48; CI 1.13, 1.96 Medical conditions during pregnancy: Gestational diabetes mellitus: OR = 4.46; CI 2.24, 9.26 **Results: non-Native Caucasian Canadian births (OR; 95% CI)** Age: (per 5 years): OR = 1.15; CI 1.05, 1.27 Genetic & Constitutional Factors: Pregravid weight (per 5 kg): OR = 1.22; CI 1.18, 2.26 Height (per 5 cm increase): OR = 1.35; CI 1.26, 1.46 Net rate of weight gain per 0.1 kg/week: OR = 1.35; CI 1.26, 1.44 Lifestyle: Smoking: OR 0.51; CI 0.39, 0.66 Obstetric history: Multiparity: OR = 1.42; CI 1.14, 1.76	Increased risk of giving birth to an infant weighing > 90th percentile for Cree women with high pregravid weight and height, and gestational diabetes mellitus. Among non-Native women, increased risk in older women, women with high pregravid weight, weight gain, increasing maternal height, and multiparity. In all macrosomic cases, the population attributable fraction for gestational diabetes mellitus was 13% among the Cree but was not a significant risk factor for non-Native women. Pregravid obesity accounted for 24% of macrosomic births among the Cree and 12% among the non-Natives. In all analyses, results were very similar for birth weight > 4,000 g or > 4,500 g.

(table continues)

Surkan, P., Hsieh, C., Johansson, A., Dickman, P., & Cnattingius, S. (2004). ***Reasons for increasing trends in large for gestational age births.***

Study setting & sample	Purpose	Results	Conclusions
Sweden N = 874,163 women who delivered a live, singleton, term infant without malformations between 1992-2001. A population-based study.	To describe the magnitude of change in the proportion of term and postterm LGA infants born between 1992 and 2001 and to examine whether time trends in prevalence of LGA births can be explained by changes in maternal risk factors. **Method:** a population-based retrospective cohort study using data obtained from the Swedish Birth Registry that is maintained by the Board of Health and Welfare. Information in this electronic file is recorded prospectively from the first prenatal visit. Risk factors included: calendar year of birth, parity, maternal age, body mass index (BMI), maternal height, cohabitating with the infant's father or not, mother's country of birth, maternal smoking, gestational diabetes, pre-eclampsia, gestational age. Outcome Variable: an LGA birth (defined as a birth weight > 2 *SD* above the mean birth weight for gestational age according to the Swedish Reference Curve for fetal growth). Term gestation was defined as 37-41 weeks' gestation; post-term gestation was ≥ 42 weeks. Control group not clearly identified in study but assumed to be normal term birth weight infants (10th-90th percentile). Adequate control of potential covariates by unconditional logistic regression.	**(OR; 95% CI):** Age: ≤ 24 years: OR = 1.06; CI 1.01, 1.10 Genetic/ constitutional: BMI > 25-29.9 (kg/m^2): OR = 1.96; CI 1.90, 2.02 BMI ≥ 30 (kg/m^2): OR = 3.28; CI 3.16, 3.41 Height ≥ 170 cm: OR = 1.86; CI 1.81, 1.91 Lifestyle: Smoking (cigarettes per day): 1-9: OR 0.52; CI 0.49, 0.55 ≥ 10: OR 0.39; CI 0.36, 0.41 Obstetric history: Parity = 2: OR = 2.19; 2.11, 2.27 Parity = 3: OR = 2.82; 2.70, 2.93 Parity = 4: OR = 3.16; 2.98, 3.36 Parity ≥ 5: OR = 3.23; CI 2.99, 3.49 Medical conditions during pregnancy: Gestational diabetes mellitus: OR = 3.35; CI 3.08, 3.63 Pregnancy complications: Pre-eclampsia: OR = 1.17; CI 1.08, 1.26	Factors that increase the risk of giving birth to an LGA infant include younger maternal age, high BMI, increasing maternal height, not smoking, increasing parity, and gestational diabetes. Increasing trends in LGA rates was explained by concurrent increases in maternal BMI and decreases in maternal smoking prevalence.

(table continues)

Okun, N., Verma, A. N., Mitchell, R. F., & Flowerdew, G. (1997). ***Relative importance of maternal constitutional factors and glucose intolerance of pregnancy in the development of newborn macrosomia.***

Study setting & sample	Purpose	Results	Conclusions
Canada n = 1,000 singleton term deliveries (≥ 36 weeks) without congenital anomalies or infections, and whose mothers had no pre-existing medical conditions known to have an effect on fetal growth and documented results of a 50 g glucose tolerance test at 24-28 weeks of pregnancy, between January 1993 and December 1993. A hospital-based study.	To determine the relative importance of various predictors of newborn macrosomia, with particular reference to maternal constitutional factors and glucose intolerance of pregnancy. **Method:** a hospital-based retrospective case-control study. Data collected by chart review of provincial prenatal and delivery records as well as diabetic clinic records, and a short interview with the mother. Mother/newborn pairs were consecutively recruited within 24-48 hours of delivery from two tertiary referral hospitals in Edmonton, Alberta. Risk factors included: age, maternal birth weight, prepregnancy weight, height, weight gain, smoking, parity, Aboriginal ethnicity, glucose tolerance, gestational age, and infant gender. Outcome Variable: term delivery of a high birth weight baby (defined as birth weight ≥ 4,000 g and ≥ 90th percentile). Controls included term infants with birth weight < 4,000 g and 10th-90th percentile, respectively. Adequate control of potential covariates by multivariate logistic regression.	**(OR; 95% CI):** **Birth weight ≥ 4,000g** Age: < 17 years vs. 17-40 years (reference): OR = 2.80; CI 1.10, 7.00 Genetic & Constitutional Factors: Prepregnancy weight: OR = 1.50/15 kg; CI 1.30, 1.80 Weight gain: OR = 1.70/7 kg; CI 1.67, 1.78 Height: OR = 1.30/7 cm; CI 1.03, 1.50 North American Aboriginal: OR = 2.90; CI 1.60, 5.30 Maternal birth weight of < 4 kg vs. > 4 kg (reference): OR = 2.20; CI 1.40, 3.60 Lifestyle: Smoking 5 cigs/day: OR = 0.70; CI 0.60, 0.80 Obstetric history: Multiparity: OR = 2.30; CI 1.50, 3.20 Infant characteristics: Gestational age of > 40 vs. < 40 weeks: OR = 2.00; CI 1.40, 2.70 Male gender: OR = 2.00; CI 1.40, 2.80	Increased risk of giving birth to an infant weighing ≥ 4,000 g and ≥ 90th percentile for mothers with high prepregnancy weight, high pregnancy weight gain, increasing height, North American Aboriginal ethnicity, and multiparity. Although there was a wide CI, maternal age < 17 years was a significant risk factor for birth weight ≥ 4,000 g but not for birth weight ≥ 90th percentile. Glucose screen positive/100-g and oral glucose tolerance test negative was significantly associated with birth weight ≥ 90th percentile but not birth weight ≥ 4,000 g. Maternal genetic and constitutional factors were the most powerful predictors of newborn macrosomia.

(table continues)

Okun, N., Verma, A. N., Mitchell, R. F., & Flowerdew, G. (1997). ***Relative importance of maternal constitutional factors and glucose intolerance of pregnancy in the development of newborn macrosomia.***

Study setting & sample	Purpose	Results	Conclusions
		Results continued (OR; 95% CI): **Birth weight ≥ 90th percentile (LGA)** Genetic & Constitutional Factors: Prepregnancy weight: OR = 1.57/15 kg; CI 1.35, 1.80 Weight gain: OR = 1.56/7 kg; CI 1.30, 1.86 Height: OR = 1.30/7 cm; CI 1.04, 1.50 North American Aboriginal: OR = 2.80; CI 1.50, 5.00 Maternal birth weight of < 4 kg vs. > 4 kg (reference): OR = 2.10; CI 1.30, 3.50 Lifestyle: Smoking: 5 cigs/day: OR = 0.66; CI 0.56, 0.78 Obstetric history: Multiparity: OR = 2.30; 1.50, 3.50 Medical conditions during pregnancy: Glucose screen positive/100-g and oral glucose tolerance test negative: OR = 1.70; CI 1.30, 2.20	

(table continues)

Orskou, J., Henriksen, T. B., Kesmodel, U., & Secher, N. J. (2003). ***Maternal characteristics and lifestyle factors and the risk of delivering high birth weight infants.***

Study setting & sample	Purpose	Results	Conclusions
Denmark n = 24,093 singleton pregnancies of non-diabetic women seeking routine antenatal care at Aarhaus University Hospital between January 1990 and December 1999. A hospital-based study.	To identify factors associated with an increased risk of giving birth to infants weighing > 4,000 g, and to determine if changes in these factors explained increasing high birth weight rates. **Method:** a hospital-based prospective cohort study. Data collected using 2 self-administered questionnaires (at 16 wks gestation), birth registration forms and medical records. Risk factors included: prepregnancy maternal weight, maternal height, age, parity, smoking habits, alcohol consumption, caffeine intake, marital status, educational level, gestational age, and infant gender. Outcome Variable: delivery of a high birth weight baby (defined as a birth weight > 4,000 g). Control group not clearly identified in study but assumed to be normal birth weight infants (2,500-3,999g) born at 40 weeks gestation. Adequate control of potential covariates by multivariate logistic regression.	**(OR; 95% CI):** Genetic & Constitutional Factors: High prepregnancy weight 70-79 kg: OR = 1.46 CI 1.33, 1.61 ≥ 80 kg: OR = 1.91; CI 1.69, 2.16 Maternal height 181-190 cm : OR = 1.21; CI 1.11, 1.33 > 190 cm: OR = 1.37; CI 1.23, 1.52 Lifestyle: Smoking (cigarettes per day) 1-4: OR = 0.74; CI 0.61, 0.89 5-9: OR = 0.51; CI 0.43, 0.60 10-14: OR = 0.42; CI 0.36, 0.50 ≥ 15: OR = 0.33; CI 0.26, 0.42 *Low level caffeine intake (≤ 200 mg/day) *High education level (> 10 years) Obstetric history: Parity = 1: OR = 1.97; CI 1.81, 2.13 Parity = 2: OR = 2.88; CI 2.56, 3.25 Parity ≥ 3: OR = 2.83; CI 2.24, 3.59 Infant characteristics: Gestational age = 39 weeks: OR = 1.95; CI 1.74, 2.17 Gestational age = 41 weeks: OR = 3.27; CI 2.93, 3.66 Gestational age ≥ 42 weeks: OR = 4.89; CI 4.31, 5.55 *Male infant gender	Increased risk of giving birth to an infant weighing > 4,000 g for women with high maternal prepregnancy weight and height, high parity, low caffeine intake, > 10 years of education, non-smoking, high gestational age, and male infant gender. Increasing high birth weight rates explained by changes in risk factor prevalence over time. Using different cutoffs for high birth weight (4,500 g instead of 4,000 g) did not alter results; risk estimates remained the same; same risk factors but less precision on the estimates using 4,500 g (n = smaller).

(table continues)

Stotland, N., Caughey, A. B., Breed, E. M., & Escobar, G. J. (2004). ***Risk factors and obstetric complications associated with macrosomia.***

Study setting & sample	Purpose	Results	Conclusions
USA *n* = 146,526 singleton live births from 1995-1999. A retrospective study of privately insured patients.	To characterize the epidemiology of macrosomia (birth weight ≥ 4,000 g and birth weight ≥ 4,500 g) and related maternal complications. **Method:** a retrospective cohort study of privately insured patients, using chart reviews and linked maternal and neonatal records obtained from the Kaiser Permanente Medical Care Program Northern California Region database and the State of California Birth Certificate Database. Risk factors included: maternal age, maternal race, parity, gestational age > 41 weeks, hypertension, diabetes mellitus (before and during pregnancy), and infant gender. Outcome Variable: delivery of a high birth weight baby (defined as a birth weight ≥ 4,000 g or ≥ 4,500 g). Control group not clearly defined but included "all birth weights." Adequate control of potential covariates by multivariate logistic regression.	**(OR; 95% CI): ≥ 4,000 g** Age: 30-39 years: OR = 1.11; CI 1.07, 1.14 Genetic/ constitutional: *white race Obstetric history: Multiparity: OR = 1.65; CI 1.60, 1.71 Medical conditions during pregnancy Gestational diabetes mellitus: OR = 1.70; CI 1.60, 1.81 Infant characteristics: Gestational age > 41 weeks: OR = 3.39; CI 3.14, 3.66 Male infant gender: OR = 1.65; CI 1.60, 1.70 **(OR; 95% CI): ≥ 4,500 g** Age: 30-39 years: OR = 1.16; CI 1.07, 1.25 Genetic/ constitutional: *white race Obstetric history: Multiparity: OR = 1.75; CI 1.62, 1.89 Medical conditions during pregnancy Gestational diabetes mellitus: OR = 2.50; CI 2.23, 2.81 Infant characteristics: Gestational age > 41 weeks: OR = 4.15; CI 3.64, 4.73 Male infant gender: OR = 1.85; CI 1.72, 1.99	Increased risk of giving birth to a macrosomic infant (birth weight ≥ 4,000 g and birth weight ≥ 4,500 g) in older women. Other risk factors included maternal race, parity, gestational age > 41 weeks, diabetes mellitus, and infant gender.

***Investigators report an increased risk but do not report the magnitude of the OR.**

Despite the rising incidence of mean birth weight and high birth weight deliveries in several developed countries including the USA, Canada, Sweden, and the UK, few epidemiologic research studies were found that focused on the macrosomic or LGA neonate. Studies on high birth weight deliveries have focused primarily on describing secular trends in the proportion of infants with excessive birth weight and maternal and neonatal complications associated with the birth of an overgrown fetus. Fewer studies in comparison were found in which relevant risk factors (predictors of high birth weight deliveries) in different populations were examined.

Both modifiable and non-modifiable risk factors that have been reported to have an association with high birth weight were examined in this literature review. The studies included in this analysis were limited to (a) cohort or case-control studies in which risk factors for both neonatal macrosomia or LGA births were specifically examined and (b) studies that controlled for potential covariates and reported adjusted ORs, relative risks, or population-attributable risks. The findings from this literature review were organized into the following risk factor categories: maternal age, genetic and constitutional factors, lifestyle factors, pre-existing medical diseases, obstetrical history, medical problems during pregnancy, pregnancy complications, and infant characteristics. Finally, a hypothetical model of risk factors was developed to guide the order of entry of variables into the risk modeling procedure using logistic regression for data analysis (White, 2004).

Defining High Birth Weight (Macrosomia, or LGA Births)

Despite systematic investigation over the years, the complex phenomenon of fetal growth is still not fully understood (Parretti et al., 2001). Birth weight is primarily a function of two factors: the rate of fetal growth and the gestational age at delivery (Leon, Johansson, & Rasmussen, 2000). The preliminary cause of growth is genetic, and the growth potential of the developing fetus is influenced by several factors, including the adequacy of the maternal intrauterine environment, the functioning of the placenta, and the availability of nutrients to both mother and fetus (Langer, 2000). Both endogenous and extrinsic effects can influence fetal weight. These include genetic (e.g., stature), ethnic (e.g., race), physiologic (e.g., fetal hormones, selected amino acids, free fatty acids, altered glucose metabolism, vascular integrity), pathologic (e.g., uterine malformations, hypertension), and environmental factors (e.g., altitude, availability of adequate nutrition, socioeconomic status). Consequently, several characteristics can affect birth weight.

Genetic control of cell growth and differentiation is the basic determinant of size at birth (Langer, 2000). In addition, fetal hormones within fetal circulation (e.g., insulin, insulin-like growth factors) help to regulate substrate availability (e.g., selected amino acids, free fatty acids, and mainly glucose) in response to nutritional and metabolic indicators. For example, uncontrolled maternal diabetes mellitus is commonly associated with excessive fetal weight because glucose is the primary substrate used for fetal growth, and when maternal glucose levels are excessive, abnormally high rates of fetal growth can be expected. When glucose diffuses across the placenta, the excess carbohydrate stimulates insulin secretion in the fetus. Insulin is the only fetal hormone that is related to intrauterine growth; therefore fetal hyperinsulinemia causes direct growth stimulation, increased cellular glucose utilization, increased fat deposition and decreased fat mobilization, and increased protein production. Insulin also stimulates absorption of amino acids into protein. Collectively, these mechanisms result in an overgrown fetus (Langer, 2000).

The two terms used to characterize high birth weight deliveries are *fetal or neonatal macrosomia* and *large for gestational age* (LGA). Researchers have used both crude (absolute) and centile (relative) birth weights to define high birth weight and to study the impact of clinical, maternal, and fetal factors on the incidence of macrosomic or LGA births. Fetal macrosomia implies growth beyond a specific weight, usually defined as a birth weight ≥ 4,000 g or 4,500 g, regardless of gestational age (Bergmann et al., 2003; Jolly et al., 2003; Okun et al., 1997; Orskou et al., 2003; Stotland et al., 2004). Large for gestational age (LGA) births refer to infants born with birth weight beyond the 90th percentile, adjusted for gestational age and gender according to established fetal growth curves (Jolly et al.; Okun et al.; Rodrigues et al., 2000; Surkan et al., 2004).

The American College of Obstetricians and Gynecologists (2000) defined neonatal macrosomia as birth weight > 4,500 g. This definition is based on the understanding that although infant and maternal morbidity associated with fetal birth weight between 4,000 g and 4,500 g exceeds that of the general obstetric population, the risks to the mother and fetus increase substantially > 4,500 g. However, this definition has not been adopted universally, and researchers continue to use different weight definitions to define macrosomia.

If a universal cut-off point such as ≥ 4,000 g or 4,500 g is used to define high birth weight infants, the influence of variables such as gestational age, ethnic, or demographic differences in mean birth weight between various countries and/or groups of people is disregarded (Rooth, 2003). It has also been suggested that birth weight

≥ 4,000 g may be considered normal for tall women (Bergmann et al., 2003). Consistent birth weight cut-offs that are associated with significant increases in general morbidity and mortality are still undefined (Boulet et al., 2003). Moreover, some researchers have demonstrated that using different cut-offs for high birth weight (i.e., ≥ 4,500 g instead of ≥ 4,000 g) did not alter the risk estimates in examining maternal factors associated with high birth weight deliveries (Orskou et al., 2003; Rodrigues et al., 2000).

In an attempt to distinguish between birth weight cut-offs that represent significant increases in general morbidity and mortality and to demonstrate that adverse outcomes differ across varying birth weight thresholds, researchers have proposed that "grades" of risk based on infant birth weight be considered (Boulet et al., 2003). These are grade 1 for infants with a birth weight between 4,000 g and 4,499 g, grade 2 for infants with a birth weight between 4,500 g and 4,999 g, and grade 3 for infants with a birth weight ≥ 5,000 g. These investigators found that grade 2 birth weight was more predictive of neonatal morbidity, whereas grade 3 birth weight was a better indicator of infant mortality. On the other hand, absolute birth weight does not reflect the impact of gestational age on birth weight and the accompanying risk of macrosomic or LGA births. Defining high birth weight as LGA offers a partial solution by considering the important influence of gestational age on birth weight (Berard et al., 1998).

The unsuccessful establishment of a universally accepted standard definition of high birth weight makes it difficult to make direct comparisons across studies, which has led to some confusion in the literature (Boulet et al., 2003). For example, differences in definitions of what constitutes a high birth weight delivery have resulted in conflicting or inconsistent findings across some studies, including the quantification of the strength of the association between relevant risk factors and high birth weight. For example, some study investigators found no gestational age effect for increased risk of delivering an LGA infant (Okun et al., 1997; Rodrigues et al., 2000; Surkan et al., 2004), whereas others found that the risk of delivering a macrosomic infant ≥ 4,000 g increased twofold to fivefold as gestational age exceeded 40 weeks (Bergmann et al., 2003; Okun et al., 1997; Orskou et al., 2003; Stotland et al., 2004).

The prenatal diagnosis of high birth weight remains imprecise, and an accurate measurement can be made only by weighing the neonate after delivery. Nonetheless, some researchers have reported that crude birth weight is a better predictor of morbidity associated with parturition and fetal morbidity, whereas centile birth weight is more useful for examining etiology and outcomes where gestational age has a significant confounding effect (Jolly et al., 2003). Based on these findings, high birth weight infants in this study were classified using centile birth weight. Consequently, an LGA infant has a birth weight > 90th percentile using the population-based Canadian reference standard for fetal growth (Kramer et al., 2001). However, this classification does not control for variations in birth weight associated with ethnicity.

From a public health perspective, identifying risk factors for high birth weight deliveries may influence strategies for preventing perinatal pathology in mothers and infants alike (Orskou et al., 2003). For instance, targeted population-based prevention programs and interventions aimed at risk reduction and health promotion in pregnant women may be helpful in reducing health risks before problems arise. It is therefore necessary to understand the etiology of high birth weight deliveries and to identify both modifiable and non-modifiable risk factors as well as their prevalence in the study population and the associated risks.

Risk-Factor Epidemiology

High birth weight is a consequence of complex interactions between fetal, placental, and maternal factors (Evers, de Valk, Mol, ter Braak, & Visser, 2002). However, much of the variation in birth weight remains unexplained, and most infants with birth weight ≥ 4,500 g have no identifiable risk factors (American College of Obstetricians and Gynecologists, 2000). In addition, the presence of identified risk factors does not necessarily result in a high birth weight infant (Raio et al., 2003). Moreover, not all high birth weight infants are equally at risk for severe complications (Boulet et al., 2003; Langer, 2000; Lipscomb et al., 1995; Orskou et al., 2003). Maternal factors that have been empirically associated with excessive fetal weight include multiparity, increased maternal weight and height, ethnic origin, diabetes mellitus, excessive maternal weight gain during pregnancy, and prolonged gestation (Langer, 2000).

Overall, few investigators have examined the epidemiology of neonatal macrosomia or LGA births. The majority of the studies conducted were European (Bergmann et al., 2003; Jolly et al., 2003; Orskou et al., 2003; Surkan et al., 2004). Of the other studies included in this review, one was conducted in the USA (Stotland et al., 2004), and two were completed in Canada (Okun et al., 1997; Rodrigues et al., 2000). The characteristics and results of the studies included in the literature review are detailed in Table 1.

In all of the studies included in the literature review, the investigators controlled simultaneously for other risk factors and covariates using multivariable unconditional logistic regression. These investigations differed in terms of the study design used (case control or cohort), the study sample (hospital vs. population-based recruitment of subjects) and sample size, the use of crude versus centile definitions of high birth weight, the data sources used to collect information on exposure variables, and the variables included in the risk models and their operational definitions.

Four studies were population-based (Bergmann et al., 2003; Jolly et al., 2003; Rodrigues et al., 2000; Surkan et al., 2004); two of the studies recruited their subjects from hospital-based cohorts (Okun et al., 1997; Orskou et al., 2003); and one study, which was conducted in the USA (Stotland et al., 2004), included singleton live births of privately insured patients. Sample sizes ranged from $N = 385$ for a geographically defined cohort of Aboriginal (Cree) infants (Rodrigues et al.) to $N = 874{,}163$ singleton term infants without malformations born in Sweden between 1992 and 2001 (Surkan et al.). For the hospital-based studies, sample sizes varied from $n = 1{,}000$ (Okun et al.) to $n = 24{,}093$ subjects (Orskou et al.).

The smaller samples did not imply inadequate study power and were a result of a number of factors, including subject inclusion and exclusion criteria, the length of the study period, and the availability of required data. For example, Okun et al. (1997) conducted a retrospective case-control study to determine the relative importance of various predictors of newborn macrosomia, with particular reference to maternal constitutional factors and glucose intolerance in pregnancy. The subjects in this study were restricted to singleton term deliveries ≥ 36 weeks' gestational age, without congenital anomalies or infection, and the mothers had no pre-existing medical conditions known to have an effect on fetal growth. The results of a 50 g glucose tolerance test at 24 to 28 weeks of pregnancy were also required to include the mother-baby pair in this study. In addition, these researchers restricted their subject recruitment to only one year. The other hospital-based study was limited to non-diabetic pregnant women who were seeking routine prenatal care (Orskou et al., 2003). However, this study had a larger sample size because of the length of the study recruitment period (1990-1999).

Maternal Age

In all of the studies included in the literature review, the impact of maternal age and its association with the risk of delivering a high birth weight infant was examined. The majority of the studies used a cohort study design (Bergmann et al., 2003; Jolly et al., 2003; Orskou et al., 2003; Rodrigues et al., 2000; Stotland et al., 2004; Surkan et al., 2004). Only one study used a case-control design (Okun et al., 1997). Generally, the results of these studies suggest that both younger maternal age (women ≤ 24 years old) and older maternal age (women ≥ 30 years old) were positively associated with an increased risk of delivering a high birth weight infant that was defined either as a crude birth weight ≥ 4,000 g or ≥ 4,500 g, or an LGA infant whose birth weight was above the 90th percentile. Overall, the increased risk associated with maternal age was modest, with ORs ranging between 1.05 and 1.22. Among older women, the risk increased slightly with increasing maternal age.

In a hospital-based case-control study, the impact of older and younger maternal age on high birth weight deliveries was investigated using both crude (≥ 4,000 g) and centile definitions (≥ 90th percentile) of high birth weight (Okun et al., 1997). Okun et al. found that younger women aged < 17 years old were nearly three times more likely to deliver an infant weighing ≥ 4,000 g (OR 2.80; CI 1.10, 7.00). However, there was no maternal age effect found when the delivery outcome was the birth of an LGA infant. This finding was not consistent with the other studies included in this review. Okun et al. suggested that their results may differ from those reported in other studies because they restricted their study to term pregnancies in healthy subjects.

In a UK study, Jolly et al. (2003) also examined the impact of maternal age using both crude (> 4,000 g) and centile (> 90th percentile) definitions for a high birth weight delivery. These researchers reported only a slightly increased risk of delivering an infant > 4,000 g for older women aged 35 to 40 years (OR 1.05; CI 1.01, 1.10). However, when high birth weight was defined using centile birth weight (> 90th percentile), the risk of delivering an LGA infant increased for both younger and older women. In addition, the risk of delivering an LGA infant among older women increased slightly as a function of maturity. The odds of delivering an LGA infant for women aged < 18 years, 35 to 40 years, and > 40 years of age were 1.19 (CI 1.01, 1.40), 1.14 (CI 1.08, 1.19), and 1.22 (CI 1.11, 1.35), respectively.

In a USA study, Stotland et al. (2004) examined the epidemiology of neonatal macrosomia among privately insured patients who delivered a singleton live-born infant between 1995 and 1999. These researchers defined high birth weight using both crude birth weight cut-offs (i.e., ≥ 4,000 g and ≥ 4,500 g), and the results for the maternal age effect were comparable. For women aged 30 to 39 years, the risk of a macrosomic delivery using birth weight ≥ 4,000 g and ≥ 4,500 g was 1.11 (CI 1.07, 1.14) and 1.16 (CI 1.07, 1.25), respectively.

Although it was shown in population-based studies that an increased risk of high birth weight deliveries ≥ 4,000 g was associated with maternal age (Bergmann et al., 2003; Jolly et al., 2003), hospital-based studies using the same high birth weight definition (≥ 4,000 g) showed no maternal age effect (Orskou et al., 2003) or maternal age effect that was limited to younger mothers < 17 years old (Okun et al., 1997). Moreover, Okun et al. reported that there was no association between maternal age and delivery of an LGA infant (see Table 1). In both of these hospital-based studies the maternal age effect in non-diabetic women was investigated, which may have influenced the study results (Okun et al., Orskou et al.). It is possible that the maternal age effect may be dependent on the clinical characteristics of the women who participated in the studies. Variations in study findings make it difficult to conduct comparisons across studies, which has led to some confusion in the literature (Boulet et al., 2003).

Genetic and Constitutional Factors

Prepregnancy Weight

The impact of maternal prepregnancy weight and its association with the risk of delivering a high birth weight infant ≥ 4,000 g or an LGA infant was examined in three studies included in the literature review. A cohort study design was used in two of the studies (Orskou et al., 2003; Rodrigues et al., 2000), and a case-control design was used in one (Okun et al., 1997). Overall, the study findings were comparable for high birth weight deliveries defined using crude birth weight cut-offs and LGA births: high prepregnancy weight increased a pregnant woman's risk of delivering a macrosomic infant with birth weight ≥ 4,000 g or an LGA infant whose birth weight was > 90th percentile. The ORs associated with maternal prepregnancy weight ranged between 1.15 and 1.91 (see Table 1).

In a prospective hospital-based study of macrosomic deliveries ≥ 4,000 g, Danish researchers examined the impact of maternal prepregnancy weight of 70 to 79 kg and > 80 kg and reported ORs of 1.46 and 1.91, respectively (Orskou et al., 2003). In another study, the risk of high birth weight deliveries was measured as a function of increments in maternal prepregnancy weight; that is, per 5 kg of weight gained (Rodrigues et al., 2000). This study population included both Cree infants and non-Native births. For every 5 kg of maternal weight gained prior to pregnancy, the risk of an LGA delivery among Cree infants compared to non-Native births increased by 1.15 and 1.22, respectively. The impact of maternal prepregnancy weight and its association with the delivery of a high birth weight infant weighing ≥ 4,000 g or an LGA birth was also examined (Okun et al., 1997). In this hospital-based case-control study, the researchers reported that for every 15 kg of maternal weight gained before pregnancy, the increased risks for delivery of a high birth weight infant weighing ≥ 4,000 g or an LGA baby were comparable, with ORs of 1.50 and 1.57, respectively.

Prepregnancy Body Mass Index (BMI)

The impact of maternal body mass index (BMI) and its association with the risk of delivering a high birth weight infant ≥ 4,000 g or > 90th percentile (LGA) was examined in three studies included in the literature review (Bergmann et al., 2003; Jolly et al., 2003; Surkan et al., 2004). The BMI was calculated as weight in kilogram per height in meters squared and categorized as lean (< 19.9 kg/m^2), normal (20-24.9 kg/m^2), overweight (25-29.9 kg/m^2), and obese (≥ 30 kg/m^2; Surkan et al.). A retrospective cohort design was used in all of the studies, and a significant positive association between a high BMI (i.e., BMI > 25 kg/m^2) and the birth of an infant weighing ≥ 4,000 g or > 90th percentile (LGA) was reported in all of the studies.

In a retrospective population-based study in Germany, the researchers reported a fourfold increase in the risk of macrosomic deliveries (infants weighing ≥ 4,000 g) when the maternal BMI exceeded 26 kg/m^2 compared to when the BMI was 20 to 26 kg/m^2, and the OR was 1.9 (Bergmann et al., 2003). When Jolly et al. (2003) examined pregnant women with a BMI between 25 and 30 kg/m^2, the odds of delivering a high birth weight infant weighing ≥ 4,000 g increased 1.5-fold. The risk of a high birth weight delivery among infants weighing ≥ 4,000 g increased to 1.9 for women with a BMI greater than 30 kg/m^2.

The impact of a pregnant woman's BMI on the incidence of LGA deliveries was examined in two population-based retrospective cohort studies (Jolly et al., 2003; Surkan et al., 2004). Women with a BMI between 25 and 30 kg/m^2 were found to be between 1.5 (Jolly et al.) and 2.0 (Surkan et al.) times more likely to deliver an LGA infant compared with women whose BMI was in the normal range. The odds of delivering an LGA infant for women with a BMI in excess of 30 kg/m^2 increased, and the reported ORs ranged between 2.1 (Jolly et al.) and 3.3 (Surkan et al.).

The influence of BMI on high birth weight deliveries using both crude (≥ 4,000 g) and centile (> 90th percentile) definitions was examined in a population-based retrospective cohort study (Jolly et al., 2003). The investigators reported comparable risks for the different BMI categories regardless of the definition used to classify infants with high birth weight. For example, the ORs associated with the delivery of an infant who weighed ≥ 4,000 g or > 90th percentile for women with a BMI between 25 and 30 kg/m^2 were comparable at 1.54 and 1.56, respectively (see Table 1). Overall, the study findings suggest that women with a high BMI have an increased risk of delivering a high birth weight infant.

Maternal Height

The impact of maternal height and its association with the risk of delivering a high birth weight infant was examined in five studies. A cohort study design was used in four studies (Bergmann et al., 2003; Orskou et al., 2003; Rodrigues et al., 2000; Surkan et al., 2004), and a case-control design was used in one study (Okun et al., 1997). The results of the studies showed that tall stature increases a pregnant woman's risk of delivering a high birth weight infant weighing ≥ 4,000 g, ≥ 4,500 g, or LGA. The ORs associated with maternal height ranged between 1.21 and 1.94; the strength of the associations reported varied across the different studies (see Table 1).

Bergmann et al. (2003) found that pregnant women in Germany whose height was at least 165 cm had a twofold increased risk for delivering a macrosomic infant weighing ≥ 4,000 g. Surkan et al. (2004) found similar results when they examined the likelihood of LGA births in mothers who were at least 170 cm tall. However, it has also been suggested that giving birth to an infant who weighs ≥ 4,000 g may be considered normal for women of tall stature (Bergmann et al., 2003), and in Denmark (Orskou et al., 2003), women whose height exceeded 180 cm had a lower risk of delivering a macrosomic infant weighing ≥ 4,000 g than did women in Germany (ORs ranged between 1.21 [maternal height between 181-190 cm] and 1.37 [maternal height > 190 cm]). Overall, the results of the studies included in the literature review suggest that increasing maternal height is associated with a greater likelihood of delivering a macrosomic or LGA infant.

Pregnancy Weight Gain

The impact of gestational weight gain and its association with the risk of delivering a high birth weight infant was explored in three studies included in the literature review. A population-based retrospective cohort study design was used in two of the studies (Bergmann et al., 2003; Rodrigues et al., 2000), and a case-control design was used in one study (Okun et al., 1997). The results of the studies consistently reveal that the amount of weight that a woman gains during her pregnancy has an impact on whether or not she is at increased risk of delivering a high birth weight infant (defined either as macrosomic birth weight ≥ 4,000 g, or an LGA infant whose birth weight is > 90th percentile). Women who gain 10 to 16 kg and > 16 kg during their pregnancy are two and three times more likely to deliver an infant weighing > 4,000 g at birth (Bergmann et al.).

In a Canadian study of LGA births, Rodrigues et al. (2000) found that the probability of delivering an LGA infant among non-Native Canadian women increased by approximately 1.4 for every 0.1 kg gained per week over the duration of the pregnancy. However, these researchers found no association between gestational weight gain and the risk of an LGA delivery among Cree women. In a hospital-based case-control study in which both crude (≥ 4,000 g) and centile (≥ 90th percentile) definitions of high birth weight were used, Okun et al. (1997) reported that the risk of delivering a macrosomic infant (weighing ≥ 4,000 g) and an LGA baby (≥ 90th percentile) increased by 1.7 and 1.6, respectively, for every 7 kg increase in maternal weight during pregnancy.

The authors of these studies generally concluded that higher gestational weight gain increases the risk of delivering a high birth weight infant, regardless of the definition of what constitutes a high birth weight delivery.

Lifestyle Factors

Smoking

The impact of smoking and its association with the risk of a high birth weight delivery was examined in nearly all of the studies. For the majority of studies, smoking was the only lifestyle factor examined (see Table 1). A cohort study design was used in most studies (Bergmann et al., 2003; Jolly et al., 2003; Orskou et al., 2003; Rodrigues et al., 2000; Surkan et al., 2004), and a case-control design was used in one study (Okun et al., 1997). Researchers unanimously reported that pregnant women who did not smoke were more likely to deliver a high birth weight infant (defined either as a macrosomic birth weight ≥ 4,000 g or 4,500 g, or an LGA infant whose birth weight was > 90th percentile).

Bergmann et al. (2003) examined the impact of smoking status during pregnancy on macrosomic deliveries ≥ 4,000 g and reported a twofold increased risk for pregnant women who were non-smokers (OR 2.03; CI 1.93, 2.14). Orskou et al. (2003) found that smoking during pregnancy had a protective effect on macrosomic deliveries > 4,000 g, which was directly proportionate to the number of cigarettes smoked (e.g., OR 0.74 [CI 0.61, 0.89] for 1-4 cigarettes smoked per day; and OR 0.33 [CI 0.26, 0.42] for at least 15 cigarettes smoked per day). Researchers in Sweden also found that the protective effect of smoking on LGA births was directly proportionate to the number of cigarettes smoked per day (i.e., OR 0.52 [CI 0.49, 0.55] for women who smoked between 1 and 9 cigarettes per day; vs. OR 0.39 [CI 0.36, 0.41] for women who smoked 10 or more cigarettes per day). In Canada, researchers also found that smoking during pregnancy had a protective effect for LGA births: OR 0.66/5 cigarettes/day (CI 0.56, 0.78; Okun et al., 1997), and OR 0.51 (CI 0.39, 0.66) in non-Native women (Rodrigues et al., 2000). Jolly et al. (2003) also reported a protective effect for LGA births among women who smoked during pregnancy (OR 0.54; CI 0.52, 0.57). Ultimately, the likelihood of delivering a high birth weight infant (i.e., the magnitude of the resulting OR) was comparable for non-smokers regardless of the definition of high birth weight.

Preexisting Medical Diseases

Diabetes Mellitus

The influence of pre-existing maternal diabetes mellitus on the incidence of high birth weight deliveries was investigated in a population-based retrospective cohort study (Jolly et al., 2003). Jolly et al. reported that women with pre-existing diabetes mellitus were approximately two times more likely to deliver an infant weighing > 4,000 g (OR 1.81; CI 1.5, 2.19) compared with women without pre-existing diabetes mellitus. The results of the same study show that the risk of delivering an LGA infant increases sevenfold for diabetic women (OR 6.97; CI 5.96, 8.16). It is possible that the increased risk of high birth weight deliveries for women with pre-existing diabetes mellitus was not evaluated in other studies because maternal diabetes mellitus has already been firmly established and widely recognized as a cause for high birth weight deliveries (Berard et al., 1998; Boyd et al., 1983; Lapunzina, Camelo, Rittler, & Castilla, 2002; Spellacy et al., 1985).

Obstetrical History

Parity

The relationship between parity and the risk of delivering a high birth weight infant was investigated in all of the studies included in the literature review. In most studies a cohort study design was used to examine the impact of parity on birth weight (Bergmann et al., 2003; Jolly et al., 2003; Orskou et al., 2003; Rodrigues et al., 2000; Stotland et al., 2004; Surkan et al., 2004), and in one study a case-control design was used (Okun et al., 1997). A significantly positive association between parity and the delivery of a high birth weight infant was reported in the study findings.

In both population- and hospital-based studies, the researchers reported that increasing parity is associated with an increased risk of macrosomic or LGA births, with ORs ranging from 1.43 to 3.23 (see Table 1). Moreover, the results of the studies included in the literature review provide evidence that risks increase incrementally as a function of higher parity. For example, Surkan et al. (2004) reported that when parity increased from 2 to > 5, the risk of an LGA birth increased from 2.2 to 3.2, respectively. Orskou et al. (2003) also reported that parity of 1 doubled the chances of a macrosomic birth > 4,000 g (OR 1.97; 1.81, 2.13). This was not found in other studies that were reviewed.

Medical Conditions During the Current Pregnancy

Gestational Diabetes Mellitus

The impact of gestational diabetes mellitus on birth weight, and, specifically, the risk for delivering a high birth weight infant, was examined in several studies included in the literature review (Bergmann et al., 2003; Jolly et al., 2003; Rodrigues et al., 2000;

Stotland et al., 2004; Surkan et al., 2004). Overall, the results of these studies suggest that women who develop gestational diabetes mellitus are more likely to deliver a high birth weight infant (i.e., an infant weighing ≥ 4,000 g, ≥ 4500 g, or > 90th percentile). The ORs associated with gestational diabetes mellitus varied, ranging between 1.57 and 4.46 (see Table 1).

In a Canadian study the impact of gestational diabetes mellitus on the risk of LGA births among Native (Cree) and non-Native women was examined (Rodrigues et al., 2000). Compared to Cree women with normal glycemic status during pregnancy, Cree women with gestational diabetes mellitus were 4.5 times more likely to deliver an LGA infant. This effect was not found in non-Native women. The researchers noted that this was the first time that a significant interaction between ethnicity and gestational diabetes mellitus as a determinant of LGA births in a controlled analysis was reported, possibly because of differences in treatment strategies for gestational diabetes mellitus in the two groups. In a population-based study in Sweden, Surkan et al. (2004) reported a threefold increase in LGA births in women with gestational diabetes mellitus.

Pregnancy Complications

Pre-eclampsia

The association between pre-eclampsia and the delivery of an LGA infant was examined in two of the studies included in the literature review (Jolly et al., 2003; Surkan et al., 2004). In a Swedish population-based cohort study of term and postterm LGA births (*N* = 874,163) born between 1992 and 2001, it was reported that pregnant women who developed pre-eclampsia were at a slightly increased risk for delivering an LGA infant (OR 1.17; CI 1.08, 1.26) compared with non-pre-eclamptic women (Surkan et al.).

Contrary to this finding, Jolly et al. reported no association between pre-eclampsia and a risk of delivering an infant weighing ≥ 4,000 g, or an LGA infant. Consequently, the study findings for an increased risk of association between high birth weight deliveries and pre-eclampsia are limited but equivocal.

Infant Characteristics

Gestational Age

The impact of increasing gestational age (defined as ≥ 40 weeks' gestational age) and its association with the risk of delivering a high birth weight infant (i.e., birth weight ≥ 4,000 g, ≥ 4,500 g, or > 90th percentile) was reported in several of the studies included in the literature review. A cohort study design was used in three of the studies (Bergmann et al., 2003; Orskou et al., 2003; Stotland et al., 2004), and a case-control design was used in one study (Okun et al., 1997). The study results show that pregnant women who carry their fetus beyond 40 weeks' gestational age have between a twofold and a fivefold increased risk of delivering a high birth weight infant.

Generally, the results of these studies suggest that pregnancies going beyond 40 weeks' gestation are associated with a higher risk of delivering an infant weighing > 4,000 g at birth. Moreover, the risk increases incrementally for every week beyond 40 weeks' gestation. For example, Okun et al. (1997) reported a twofold increased risk of macrosomia for infants born after 40 weeks' gestational age. For infants born at 41 weeks' gestational age, Orskou et al. (2003) reported a threefold increase in risk for a macrosomic delivery ≥ 4,000 g, and for infants born at or after 42 weeks' gestation, the risks increased substantially to fivefold (Orskou et al.).

Only three studies considered the effect of increasing gestational age on the incidence of LGA births (Okun et al., 1997; Rodrigues et al., 2000; Surkan et al., 2004). In these studies a gestational age effect (i.e., ≥ 40 weeks) for LGA births was not reported.

Infant Gender

The effect of infant gender (male vs. female) on high birth weight was examined in four of the studies included in the literature review. A cohort study design was used in three of the studies to determine whether an association existed (Bergmann et al., 2003; Orskou et al., 2003; Stotland et al., 2004). In the remaining study, a case-control design was used (Okun et al., 1997). All of these investigators reported an association between male gender and the risk of high birth weight ≥ 4,000g or 4,500 g, with ORs ranging between 1.65 and 2.00 (see Table 1). Although Orskou et al. reported a significant increased risk of macrosomic deliveries (infants weighing > 4,000 g) with male infant gender, they did not quantify the magnitude of the association. Conversely, a male gender effect with LGA births was not consistently reported. In a Canadian study, Okun et al. found no association between gender and the risk of delivering an LGA infant.

Summary

Neonatal macrosomia is increasingly common and clinically important (Bonnellie & Raab, 1997). High birth weight deliveries are associated with significant obstetric morbidity and pose a potential threat for both the mother and the neonate. However, despite recognition of risk factors, it is still impossible to accurately predict neonatal macrosomia or LGA births clinically, and many of these high birth weight infants have no identifiable risk factors.

There are a number of maternal, infant, obstetric, and lifestyle factors that have a significant impact on infant birth weight. The results of the studies reviewed suggest that women are more likely to deliver high birth weight infants if they have a high prepregnant maternal BMI (≥ 30 kg/m^2), a high pre-gravid maternal weight (≥ 80 kg), a high gestational weight gain (≥ 16 kg), high parity (≥ 3), pre-existing diabetes mellitus, gestational diabetes mellitus, or are tall in stature (≥ 165 cm). Other risk factors include maternal age, post-term pregnancies, non-smoking status during pregnancy, and male infant gender. Both younger and older women are likely to deliver an infant > 4,000 g or > 90th percentile, but the risk is slightly higher in women over 40 years old (OR 1.22; CI 1.11, 1.35). There was also consensus that women who smoke are less likely to deliver a macrosomic infant. The strongest predictors for high birth weight deliveries were high maternal BMI, excessive weight gain during pregnancy, high parity, and maternal diabetes mellitus (i.e., pre-existing and gestational).

Associations between these maternal and pregnancy (clinical) factors and the delivery of a macrosomic or LGA infant were not reported in all studies. There was some inconsistency in the findings reported across the studies, including variations in the quantification of risk for a number of factors identified in the different risk models. Inconsistent findings may be a result of several methodological differences and limitations observed across the various studies included in this review. Differences include study setting and population sampled (i.e., hospital based vs. population based), failure to control for various confounders, inadequate sample size and power, inappropriate risk modeling, inconsistency in defining *high birth weight*, differing calculations of gestational age (i.e., last menstrual period vs. ultrasound dates), and incomplete and/or inaccurate data sources or lack of precision in reported diagnoses and morbidities (e.g., studies relying on birth certificate data). In addition, important confounders (e.g., parity, pre-existing diabetes mellitus, and gestational diabetes mellitus) were not controlled in a number of the studies.

Additional research is necessary to examine current trends in high birth weight deliveries and to determine the factors that significantly impact birth weight and increase the risk of delivering an infant weighing > 90th percentile in different populations. From a public health perspective, the identification of modifiable factors that are prevalent and have a moderate risk associated with them is important for the planning of population-based interventions aimed at prevention and the promotion of maternal and infant health. Identification of antenatal predictors for "at-risk" pregnancies is important to facilitate interventions that reduce risk to enable health care providers to provide suitable counseling and to effect appropriate strategies for prevention and/or management and follow-up during pregnancy and after delivery.

A Hypothetical Model of Potential Risk Factors for Large for Gestational Age Births

Based on the literature reviewed, a hypothetical model for T-LGA births was developed as outlined in the methods section in Chapter 3. It included both distal and proximal causes of LGA births—specifically, potential risk factors present prior to pregnancy (e.g., maternal demographic factors, genetic and constitutional factors, and obstetric history)—and risk factors that may exert their influence on the pregnancy or develop during the pregnancy (e.g., lifestyle factors, medical problems during the current pregnancy, and pregnancy complications). This model determined the entry of the potential risk factors into the logistic regression model.

Maternal age was assumed to be the most distal factor in this model and was entered into the logistic regression model first because several of the subsequent factors may be a function of age (i.e., genetic and constitutional factors, lifestyle factors, pre-existing medical diseases, obstetrical history, medical problems during pregnancy, and pregnancy complications). Genetic and constitutional factors, lifestyle factors, pre-existing medical diseases, and obstetrical history were entered next because they are a function of age, are present prior to the index pregnancy, and may influence the pregnancy. Similarly, lifestyle factors and pre-existing medical diseases may influence obstetrical history, and medical problems during the current pregnancy could cause pregnancy complications. Pregnancy complications were considered intermediate pregnancy outcomes and were therefore situated just prior to the infant's gestational age and gender. Gestational age was also included in the model, which assumes that post-term pregnancies are more likely to result in the delivery of a high birth weight infant.

CHAPTER 3:

METHODS

Study Design

A population-based retrospective cohort study was used to estimate the independent effects of maternal and newborn factors and pregnancy characteristics on the incidence of T-LGA births in Northern and Central Alberta. The specific study objectives were (a) to estimate T-LGA birth rates in Northern and Central Alberta from 1996 to 2003 and to determine whether these rates have changed over time; (b) to identify the modifiable and non-modifiable risk factors that increase the chances of T-LGA births to women who reside in Northern and Central Alberta (e.g., maternal age, genetic and constitutional factors, pre-existing maternal morbidity, problems during pregnancy, and lifestyle factors); (c) to quantify the relative contribution of these risk factors on the incidence of T-LGA births while simultaneously controlling for other risk factors; and (d) to determine the public health importance of significant modifiable risk factors that could be targeted in population-based prevention programs and interventions aimed at risk reduction and health promotion in pregnant women.

The potential determinants (both modifiable and non-modifiable risk factors) that had been previously cited in the published medical literature as having an impact on birth weight—and, specifically, were reported to be associated with excessive birth weight (i.e., neonatal macrosomia or LGA)—were included in the risk model.

Study Subjects

The overall study population consisted of $N = 170{,}551$ women who were residents of and gave birth in Northern and Central Alberta between January 1, 1996, and

December 31, 2003. From this population, subjects (comprised of mother-infant pairs) were selected if they met the following study inclusion criteria: birth of a singleton live-born infant 37 to 40 weeks' and six days completed gestational age at birth with no major congenital anomalies. Multiple gestation pregnancies (*n* = 1,967) and pregnancies that ended in a stillbirth (*n* = 1,156) were excluded from the analyses. Infants with congenital anomalies (*n* = 1,498), preterm births < 37 weeks' completed gestation (*n* = 13,636), post-term infants ≥ 41 weeks' completed gestation, and term small for gestational age (i.e., 37 to 40 weeks' and six days completed gestation and birth weight < 10th percentile; *n* = 34,444) were also excluded. Moreover, eligible cases were excluded if there were missing or out-of-range values for birth weight, gestational age, or infant gender (*n* = 2,652). These variables were required for the classification of births as LGA or AGA using the population-based Canadian reference standards for fetal growth (Kramer et al., 2001). After exclusions, *n* = 115,198 mother-infant pairs were included in the analysis. The cases were comprised of *n* = 15,190 (13.2%) T-LGA births, and *n* = 100,008 (86.8%) term AGA (T-AGA) births made up the control or reference group.

Data Source

This study used maternal and newborn data recorded in the Northern and Central Alberta Perinatal Database, which is one of two regional perinatal databases maintained by the Alberta Perinatal Health Program (APHP). Data are collected from health care facilities that have provided maternal-newborn care in Regional Health Authorities 6 through 17. This computerized population-based perinatal database contains the pregnancy and birth data previously recorded in the Provincial Delivery Records (Parts 1 and 2) by hospital staff at the time of delivery. These Provincial Delivery Records are completed for all deliveries.

Participating hospitals collect data from the Provincial Delivery Records from one of three sources: (a) directly from the Provincial Delivery Record, (b) from a log book that is transcribed from the Provincial Delivery Record, or (c) by electronic transfer of the data from the Provincial Delivery Record. Perinatal data are recorded based on the place of delivery, and this information is forwarded to the APHP Data Manager for data entry.

Several precautions are taken to ensure both the completeness and the accuracy of the data. The Data Manager reviews records received in paper format for discrepancies prior to data entry by the trained data entry clerk. After they are entered, a data validation process begins that consists of a monthly crosscheck of the manual tabulation of key variables with an electronic tabulation of these same variables. A minimum of 1 in 20 records is verified with the actual data entry to check accuracy. Participating hospitals are also provided with methods for validating electronic data. The APHP Data Manager completes a validation process for electronically transferred data as well. This consists of electronic tabulation and comparison with the Monthly Statistical Report that is supplied with the data.

The Northern and Central Alberta Perinatal Database includes information on genetic and constitutional factors, maternal age, pre-existing maternal diseases, obstetrical history, medical disorders and problems in the current pregnancy, lifestyle factors, pregnancy complications, birth outcomes, and selected information about the infant.

Study Variables

The variables selected for inclusion in this study were based on the review of the published medical literature. The independent variables (risk factors) that were included in the risk model for T-LGA births are presented in Table 2. These factors were categorized into the following groupings: maternal demographic characteristics, genetic and constitutional factors, lifestyle factors, pre-existing medical diseases, obstetrical history, medical problems during the current pregnancy, pregnancy complications, and infant characteristics.

Risk modeling for T-LGA births was limited to maternal and newborn data recorded in the Northern and Central Alberta Perinatal Database and the way in which the potential risk variables were measured or aggregated. Consequently, only a partial model of the risk factors that could increase a woman's risk for delivering a T-LGA baby can be provided. A full explanatory model would require further research and an examination of other potential determinants not recorded in the perinatal database used in this study.

Maternal age was defined as the woman's age in years at the time of delivery. Maternal weight was recorded as ≤ 45 kg, between 46 kg and 90 kg, and ≥ 91 kg; and maternal height was categorized as < 152 cm and ≥ 152 cm. Maternal smoking was defined as involving women who smoked at any time during the pregnancy. Maternal alcohol consumption was recorded if the women reported either ≥ 3 drinks on any one occasion or ≥ one drink per day during pregnancy. Drug use during pregnancy was defined as inappropriate or excessive use of any substance that might adversely affect the outcome of the pregnancy.

Table 2

Independent Variables (Risk Factors) Included in the Risk Model for Term Large for Gestational Age Births

Independent variables (risk factors)	Variables included in the risk model for term large for gestational age births
Maternal demographic factors	Maternal age
Genetic and constitutional factors	Maternal prepregnancy weight Maternal height
Lifestyle factors	Smoking during pregnancy Alcohol during pregnancy Drug use during pregnancy
Pre-existing medical diseases	Pre-existing diabetes mellitus
Obstetrical history	Gravidity Parity High parity for maternal age Previous LGA birth Previous stillbirth Previous neonatal death
Medical problems during current pregnancy	Gestational diabetes mellitus Hydramnios (Polyhydramnios or Oligohydramnios)
Pregnancy complications	Pregnancy-induced hypertension (PIH) Pre-eclampsia/Eclampsia
Infant characteristics	Gestational age Infant gender

Pre-existing diabetes mellitus was defined as impaired glucose tolerance treated by restriction of carbohydrate intake or glucose-lowering medication while not pregnant. Pregnancy-induced hypertension (PIH) was defined as gestational blood pressure of 140/90 mmHg or higher. Pre-eclampsia was defined as blood pressure > 140/90 mm Hg with proteinuria of at least 1+ on dipstick in two samples obtained six hours apart, or > 0.3 g in a 24-hour urine collection.

Gravidity was defined as the total number of pregnancies regardless of the duration and outcome, including the current pregnancy. Parity was defined as the number of pregnancies delivered > 20 weeks' completed gestation prior to the index pregnancy (N. Demianczuk and N. Bott, personal communication, May 19, 2005). High parity for maternal age was considered to be ≥ 1 birth for adolescents, ≥ 3 previous births for mothers 18 to 21 years old, ≥ 4 previous births for mothers 22 to 24 years old, and ≥ 5 previous births for mothers ≥ 25years old (Boulet et al., 2003).

Gestational age was based on the date of the last menstrual period, confirmed by early pelvic examination and verified by first-trimester or early second-trimester ultrasonography when available. If the date of the last menstrual period was believed to be inaccurate, the gestational age was based on the first-trimester or early second-trimester ultrasonography findings. Gender was classified as male, female, or unknown.

Classification of the Birth Outcome Variables

The outcome (dependent) variable was delivery of a singleton live-born T-LGA infant with no major congenital anomalies. An infant's gender, birth weight, and gestational age (number of completed weeks' gestation at the time of delivery) was used to classify the birth as either LGA or AGA. A T-LGA birth included babies born at 37 to 40 weeks' and six days completed gestational age with a birth weight > 90th percentile using Canadian population-based birth weight standards (Kramer et al., 2001). The reference group for comparison was T-AGA infants, which was comprised of term normosomic infants who were 37 to 40 weeks' and six days completed gestational age with a birth weight between the 10th and the 90th percentiles.

Data Analysis

APHP data were cleaned and analyzed using SPSS for Windows Version 13.0. New variables were created as required from existing variables in the APHP database using the *transform recode* command in the SPSS data analysis program.

To investigate secular trends in the incidence of LGA births, LGA rates per 1,000 live births were estimated from 1996 to 2003. A chi-square (linear trend) analysis was used to examine LGA trends (rate changes) over time. A two-sided p-value ≤ 0.05 was used to determine whether the observed trends were statistically significant.

The prevalence and distribution of the study variables were summarized by group (i.e., all births, T-LGA births, and T-AGA births) using descriptive statistics. For continuous variables, means and standard deviations (*SD*) were reported. Frequencies and percentages were used to summarize categorical variables. To determine whether the prevalence and distribution of the study variables across the study groups were different, the following univariable analyses were done: (a) student's t-test for comparison of variables measured on a continuous scale and (b) the chi-square test for differences in the proportion of T-LGA births for discrete (categorical) variables. A two-sided p-value ≤ 0.05 was used to determine if the observed differences were statistically significant.

Univariable logistic regression was used to determine the contribution of each predictor on the incidence of T-LGA births, without controlling for the influence of confounding factors. Unadjusted ORs and 95% CIs were estimated and reported to indicate the magnitude and direction of the effect of each potential risk factor on birth weight for gestational age.

Next, unconditional multivariable logistic regression (MLR) was used to determine the independent effects of each maternal and newborn predictor of T-LGA births, while simultaneously controlling for other study variables (potential confounders). Adjusted ORs and 95% CIs were estimated to determine the magnitude and direction of the effect of the study variables on birth weight controlled for gestational age.

A hypothetical risk model was developed for T-LGA births. Predictor variables were entered into the logistic regression model in a stepwise fashion in blocks as outlined in Figure 1 (White, 2004). The ordering of the blocks of variables corresponded to variables relating to the mother before pregnancy, her obstetrical history, and problems in her current pregnancy. Pregnancy complications were entered into the risk model last, just before inclusion of infant characteristics (i.e., gestational age and infant gender). These factors were assumed to be intermediate pregnancy outcomes and, if entered earlier in the risk model, could lead to an underestimation of the effects of study factors whose impact were mediated through that pregnancy complication (Kramer, 1987; Lang, Lieberman, & Cohen, 1996).

Interaction terms were also included in the risk model. The selection of the interaction terms was based on the results of previous research studies. These interactions were entered into the risk model following the entry of the individual variables if they were found to be statistically significant during univariable analysis.

The population-attributable risk percentage (PAR%) was calculated to estimate the potential public health impact of all significant risk factors. It represented the proportionate reduction in the incidence of T-LGA births when the risk factor or its effects were eliminated (Kleinbaum, Kupper, & Morgenstern, 1982). The PAR was

Block 1 Demographics (maternal age)

↓

Block 2 Genetic and Constitutional Factors (prepregnancy weight, height)

↓

Block 3 Lifestyle Factors (smoking status, alcohol consumption during pregnancy, drug dependency)

↓

Block 4 – Interactions
Smoking by Alcohol
Smoking by Drug Dependency
Alcohol by Drug Dependency
Smoking by Alcohol by Drug Dependency

↓

Block 5 Pre-existing Medical Diseases (diabetes mellitus)

↓

Block 6 Obstetrical History (parity, gravidity, high parity for maternal age, previous LGA birth, previous stillbirth, previous neonatal death)

↓

Block 7 Medical Problems During Current Pregnancy (gestational diabetes mellitus, hydramnios (polyhydramnios or oligohydramnios)

↓

Block 8 Pregnancy Complications (pregnancy-induced hypertension (PIH))

↓

Block 9 Pregnancy Complications (PIH with proteinuria or pre-eclampsia/eclampsia)

↓

Block 10 Gestational Age (completed weeks' gestation)

↓

Block 11 Infant Gender (male vs. female)

↓

Term Large for Gestational Age Birth (T-LGA)

Figure 1. Hypothetical model of potential risk factors for term large for gestational age births and order of entry for study variables.

estimated using the following formula: $P_e (RR - 1)/1 + P_e (RR - 1)$, where P_e = proportion exposed in the population and RR = the relative risk that was estimated by the adjusted OR. Its magnitude depends on the prevalence of exposure in the population and its associated relative risk. For example, a large PAR can be a result of a high prevalence, a high RR, or both (Kleinbaum et al., 1982). Intervention was recommended for conditions with a high PAR (Berkowitz & Lapinski, 1998). Although the etiology of T-LGA births was multifactorial, it was assumed that each risk factor had exerted an independent effect when the proportion of cases that might be prevented was estimated (Walter, 1980).

Ethical Considerations

The proposal was submitted to the Ethics Review Board (Panel B) at the University of Alberta for expedited review and approval. The data for the proposed study had already been collected by the Alberta Perinatal Health Program (APHP) as part of its audit program. Approval was obtained from the APHP Data Manager for data access and secondary data analysis. To maintain the privacy and anonymity of women whose records were included, the data file that was provided to this researcher did not contain personal identifiers (only subject code numbers). Study findings were reported by group (i.e., aggregate results) to maintain subject confidentiality. Only the study investigator and the research supervisory committee had access to the data file used in this study. Data were analyzed on a secure computer network at the University of Alberta. All data will be kept secured in a locked filing cabinet at the University of Alberta for seven years.

CHAPTER 4:

RESULTS

The purpose of this study was to identify modifiable and non-modifiable risk factors that increase the likelihood of delivering a T-LGA birth in a geographically defined population and to quantify their public health importance. Of particular importance in this study was the identification of potentially modifiable risk factors that could be targeted in population-based prevention programs, as well as interventions aimed at risk reduction and health promotion in pregnant women.

A population-based retrospective cohort study was conducted using maternal and obstetric risk factor information contained in the Alberta Perinatal Health Program (APHP) perinatal database. The selection of study factors included in the risk modeling was based on a review of previous epidemiological studies that identified risk factors and exposures that increase a woman's risk of delivering a macrosomic or LGA infant. Only a partial model of the potential risk factors for T-LGA births could be developed in this study because the risk modeling was restricted to maternal and newborn data recorded in the APHP database and how they were measured or aggregated. Further research and an assessment of possible risk factors that are not currently recorded in the APHP database would be necessary to present a full explanatory model.

Study Population

The study population consisted of N = 170,551 women who were residents in Northern and Central Alberta and gave birth between January 1, 1996, and December 31, 2003. For this study only term live-born singleton births without anomalies were included. The case-control comparison was between T-LGA infants (cases) and normosomic term babies (T-AGA). Multiple births (*n* = 1,967), infants with congenital anomalies (*n* = 1,498), preterm births (*n* = 13,636), and term small for gestational age births and post-term births (*n* = 34,444) were excluded from the study cohort. Stillbirths (*n* = 1,156) and eligible cases with missing values for gestational age, birth weight, or infant gender (*n* = 2,652) were also not included in this study. After these exclusions, *n* = 115,198 mother-infant pairs were included in the data analysis to determine the predictors of T-LGA births in Northern and Central Alberta. Of these births, 13.2% (*n* = 15,190) were classified as T-LGA, and 86.8% (*n* = 100,008) were classified as T-AGA.

Table 3 summarizes the maternal, reproductive, and lifestyle characteristics of the study population. The maternal age of the study population ranged from 12 to 50 years, with a mean age of 27.8 years. Seventy-nine percent (*n* = 91,740) of all births occurred among women aged 20 to 34 years; the percentage of births occurring in younger women (≤ 19 years) and older women (≥ 35 years) was *n* = 8,406 (7.2%) and *n* = 14,232 (12.4%), respectively. Approximately 81% of the women delivered spontaneously, and slightly more than 37% (*n* = 42,897) of the study population were nulliparous (first pregnancy). Among multiparous women, *n* = 1,323 (1.1%) had previously delivered an LGA birth, *n* = 1,156 (1.0%) reported a pregnancy leading to a stillbirth, and *n* = 680 (0.6%) had lost an infant during the neonatal period. Only *n* = 2,824 women (2.5% of the study population) were classified as being high parity for age (defined as at least one birth for mothers aged ≤ 17 years, at least three previous births for mothers who were 18-21 years old, at least four previous births for women 22-24 years old, or at least five previous births for women ≥ 25 years old; Boulet et al., 2003).

Table 3

Distribution of Term Large for Gestational Age (T-LGA) and Term Appropriate for Gestational Age (T-AGA) Infants According to Maternal and Infant Characteristics

Characteristics	**All births** ***N* = 115,198** *N* (%)	**T-AGA** ***n* = 100,008** *n* (%)	**T-LGA** ***n* = 15,190** *n* (%)
Maternal age (years) (mean ± *SD*)	**27.81 ± 5.62**	**27.71 ± 5.62**	**28.46 ± 5.57**
*** Maternal age (years)**			
≤ 17	2,820 (2.4)	2,518 (2.5)	302 (2.0)
18 – 19	5,586 (4.8)	5,052 (5.1)	534 (3.5)
20 – 29	61,612 (53.5)	53,901 (53.9)	7,711 (50.8)
30 – 34	29,858 (25.9)	25,560 (25.6)	4,298 (28.3)
35 – 39	12,170 (10.6)	10,290 (10.3)	1,880 (12.4)
≥ 40	2,062 (1.8)	1,734 (1.7)	328 (2.2)
Missing data	1,090 (0.9)	953 (1.0)	137 (0.9)
Genetic or constitutional factors			
Maternal prepregnancy weight (kg)			
≤ 45	396 (0.3)	346 (0.3)	50 (0.3)
46-90	102,631 (89.1)	90,378 (90.4)	12,253 (80.7)
* ≥ 91	9,534 (8.3)	6,958 (7.0)	2,576 (17.0)
Missing data	2,637 (2.3)	2,300 (2.3)	311 (2.0)
Maternal height (cm)			
< 152	1,996 (1.7)	1,831 (1.8)	165 (1.1)
* ≥ 152	110,571 (96.0)	95,857 (95.8)	14,714 (96.9)
Missing data	2,631 (2.3)	2,320 (2.3)	311 (2.0)
Lifestyle factors during pregnancy			
*Smoking			
No	84,306 (73.2)	72,072 (72.1)	12,234 (80.5)
Yes	28,261 (24.5)	25,617 (25.6)	2,644 (17.4)
Missing data	2,631 (2.3)	2,319 (2.3)	312 (2.1)
Use of alcohol			
No	110,444 (95.9)	95,790 (95.8)	14,654 (96.5)
Yes	2,120 (1.8)	1,896 (1.9)	224 (1.5)
Missing data	2,634 (2.3)	2,322 (2.3)	312 (2.1)
Use of street drugs			
No	111,630 (96.9)	96,819 (96.8)	14,811 (97.5)
Yes	933 (0.8)	866 (0.9)	67 (0.4)
Missing data	2,635 (2.3)	2,323 (2.3)	312 (2.1)

(table continues)

Characteristics	All births *N* = 115,198 *N* (%)	T-AGA *n* = 100,008 *n* (%)	T-LGA *n* = 15,190 *n* (%)
Pre-existing medical diseases			
*Diabetes mellitus			
No	111,671 (96.9)	97,088 (97.1)	14,583 (96.0)
Yes	895 (0.8)	600 (0.6)	295 (1.9)
Missing data	2,632 (2.3)	2,320 (2.3)	312 (2.1)
Obstetrical history			
* Parity			
0 (nulliparous)	42,897 (37.2)	38,739 (38.7)	4,158 (27.4)
1	41,393 (35.9)	35,479 (35.5)	5,914 (38.9)
2	18,595 (16.1)	15,697 (15.7)	2,898 (19.1)
3	6,832 (5.9)	5,610 (5.6)	1,222 (8.0)
≥ 4	4,697 (4.1)	3,816 (3.8)	881 (5.8)
Missing data	784 (0.7)	667 (0.7)	117 (0.8)
* High parity for maternal age†			
No	110,578 (96.0)	96,159 (96.2)	14,419 (94.9)
Yes	2,824 (2.5)	2,295 (2.3)	529 (3.5)
Missing data	1,796 (1.6)	1,554 (1.6)	242 (1.6)
* Gravidity			
1	33,268 (28.9)	30,057 (30.1)	3,211(21.1)
2-4	70,873 (61.5)	60,828 (60.8)	10,045 (66.1)
≥ 5	11,040 (9.6)	9,106 (9.1)	1,934 (12.7)
Missing data	17 (0.0)	17 (0.0)	0 (0.0)
* History of LGA birth			
No	111,240 (96.6)	97,015 (97.0)	14,225 (93.6)
Yes	1,323 (1.1)	670 (0.7)	653 (4.3)
Missing data	2,635 (2.3)	2,323 (2.3)	312 (2.1)
History of stillbirth			
No	111,408 (96.7)	96,716 (96.7)	14,692 (96.7)
Yes	1,156 (1.0)	970 (1.0)	186 (1.2)
Missing data	2,634 (2.3)	2,322 (2.3)	312 (2.1)
* History of neonatal death			
No	111,884 (97.1)	97,124 (97.1)	14,760 (97.2)
Yes	680 (0.6)	562 (0.6)	118 (0.8)
Missing data	2,634 (2.3)	2,322 (2.3)	312 (2.1)

(table continues)

Characteristics	All births $N = 115{,}198$ N (%)	T-AGA $n = 100{,}008$ n (%)	T-LGA $n = 15{,}190$ n (%)
*** Medical problems during current pregnancy**			
Gestational diabetes mellitus			
No	109,136 (94.7)	95,062(95.1)	14,074 (92.7)
Yes	3,428 (3.0)	2,624 (2.6)	804 (5.3)
Missing data	2,634 (2.3)	2,322 (2.3)	312 (2.1)
Hydramnios (polyhydramnios or oligohydramnios)			
No	111,104 (96.4)	96,494 (96.5)	14,610 (96.2)
Yes	1,460 (1.3)	1,192 (1.2)	268 (1.8)
Missing data	2,634 (2.3)	2,322 (2.3)	312 (2.1)
*** Pregnancy complications**			
Pregnancy induced hypertension (PIH) or Pre-eclampsia/eclampsia			
No	110,163 (95.6)	95,821 (95.8)	14,342 (94.4)
Yes			
PIH	3,936 (3.4)	3,252 (3.3)	684 (4.5)
Pre-eclampsia/eclampsia	1,099 (1.0)	935 (0.9)	164 (1.1)
Infant characteristics			
Gender			
Female	56,408 (49.0)	48,901 (48.9)	7,507 (49.4)
Male	58,790 (51.0)	51,107 (51.1)	7,683 (50.6)
Gestational age (weeks)			
37	9,380 (8.1)	8,097 (8.1)	1,283 (8.4)
38	23,768 (20.6)	20,502 (20.5)	3,266 (21.5)
39	37,263 (32.3)	32,504 (32.5)	4,759 (31.3)
40	44,787 (38.9)	38,905 (38.9)	5,882 (38.7)

* Significant $p < 0.001$

† High parity for age was defined as ≥ 1 birth for mothers ≤ 17 yrs, ≥ previous 3 births for mothers 18-21 yrs, ≥ 4 previous births for mothers 22-24 yrs, ≥ 5 previous births for mothers ≥ 25 yrs

Approximately $n = 28{,}261$ or 25% of the women reported that they had smoked during their pregnancy; $n = 2{,}861$ (1.8%) reported the consumption of alcohol during their pregnancy; and $n = 933$ (0.7%) of the study population indicated that they had used street (recreational) drugs during their pregnancy. The percentage of missing data for these lifestyle factors was low (2.3%). However, it was assumed that the rates of drug and alcohol use during pregnancy were underestimated because of reporting bias and misclassification of exposure by study subjects. The majority of the women in the study cohort—$n = 102,631$ (89%)—reported a prepregnancy weight between 46 and 90 kg; $n = 9,534$ (8.3%) were classified as obese, with a prepregnancy weight of ≥ 91 kg.

The majority of women who delivered in the study period had no pre-existing medical diseases. Only $n = 895$ (0.8%) of the women were diabetic and using insulin. Three percent of the study population developed gestational diabetes, 3.4% were diagnosed with pregnancy induced hypertension (PIH), and 1% was classified as having pre-eclampsia/eclampsia.

The mean birth weight was 3,529 g (*SD* ± 423 g), the mean gestational age was 39.02 weeks (*SD* ± 0.96 weeks), and 51% of the infants ($n = 58,790$) were male. The majority of births—$n = 82,050$ (71%)—occurred after 39 weeks gestational age.

Secular Trends in Large for Gestational Age Births

The prevalence of all LGA births, preterm LGA (P-LGA) births, T-LGA births, and postterm LGA(PT-LGA) births in the study population is presented in Figure 2. During the study period the overall LGA birth rate increased from 11.3% in 1996 to 12.5% in 2003. The proportion of T-LGA births also increased substantially over the same period, from 8.6% in 1996 to 9.9% in 2003. The chi-square test for linear trend for all LGA births and T-LGA births was statistically significant ($p < 0.001$). The chi-square tests for linear trend for P-LGA births ($p < 0.095$) and PT-LGA births ($p < 0.131$) did not show a significant increase over the follow-up period. These results suggest that it is the increasing proportion of T-LGA births that is resulting in the overall increase in the LGA birth rate.

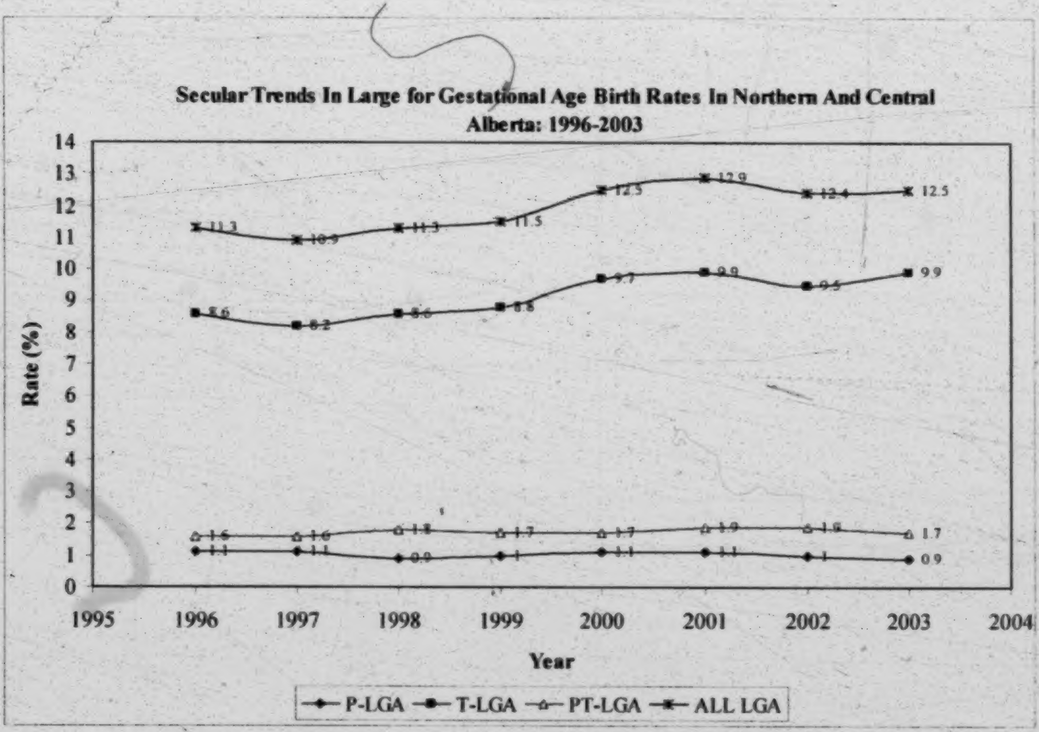


Figure 2. Secular trends in large for gestational age birth rates in Northern and Central Alberta: 1996-2003.

Prevalence of Maternal, Reproductive, and Infant Characteristics in Term Large for Gestational Age (T-LGA) and Term Appropriate for Gestational Age (T-AGA) Births

The prevalence of maternal, reproductive, and infant characteristics by birth outcome (T-LGA births [cases] compared with T-AGA births [controls]) were organized into the following categories: maternal age, genetic or constitutional factors, lifestyle factors, pre-existing medical diseases, obstetrical history, medical problems during pregnancy, pregnancy complications, and infant characteristics. The prevalence and distribution of these characteristics are shown in Table 3. Only a small proportion of data were missing overall; the highest proportion of missing data in any individual risk category was 2.3% (*n* = 2,650; see Table 3).

There was an increased prevalence of T-LGA births for the majority of the study variables for the designated high-risk exposure categories. The mean maternal age for women delivering a T-LGA baby was slightly higher than for women who delivered a T-AGA baby (28.5 ± 5.6 years vs. 27.7 ± 5.6 years). A higher proportion of women who gave birth to a T-LGA baby were 35 years of age and older (14.6% [*n* = 2,218] vs. 12% [*n* = 12,024]), had a prepregnancy weight ≥ 91 kg (17% [*n* = 2,576] vs. 7% [*n* = 6,958]), were multiparous and had delivered three or more children previously (13.8% [*n* = 2,103] vs. 9.4% [*n* = 9,426]), were diabetic (1.9% [*n* = 295] vs. 0.6% [*n* = 600]), had delivered an LGA infant in a previous pregnancy (4.3% [*n* = 653] vs. 0.7% [*n* = 670]), and were classified as high parity for maternal age (3.5% [*n* = 529] vs. 2.3% [*n* = 2,295]). Moreover, women who delivered a T-LGA infant were more likely to experience medical problems during their pregnancy, as well as pregnancy complications. For example, 5% (*n* = 804) of women who delivered a T-LGA baby developed gestational diabetes in the index pregnancy compared with only 2.6% (*n* = 2,624) of women who gave birth to a T-AGA baby. The proportion of women with pregnancy-induced hypertension (PIH) was 4.5% (*n* = 684) and 3.3% (*n* = 3,252) for women delivering T-LGA and T-AGA infants, respectively, and a higher proportion of women who gave birth to a T-LGA baby had pre-eclampsia/eclampsia (1.1% vs. 0.9%).

Predictors of Term Large for Gestational Age Births:

Odds Ratios and 95% Confidence Intervals

A hypothetical risk model of potential risk factors for T-LGA births was developed a priori based on an extensive review of previously conducted risk factor studies. This model was used to provide direction for the modeling of risk factors for T-LGA births (Figure 1). It represents the ordering of the risk factors for entry into the multiple logistic regression (MLR) analysis. This order considers the proximal and distal relationship of the risk factors as well as the relationship between the risk factors and the birth outcome (White, 2004).

First, the crude (unadjusted) ORs and 95% CIs were calculated for each study variable to estimate the magnitude and direction of the effect of each potential risk factor on the incidence of T-LGA births (Table 4). An OR estimates the risk of delivering a T-LGA birth in women who were exposed to the risk variable compared to the risk for women who were not exposed.

In the univariable analysis, T-LGA births occurred more frequently among women who were over 30 years of age (ORs ranged between 1.18 and 1.32), ≤ 17 years old (OR 1.84; CI 1.70, 1.90), obese (prepregnancy weight ≥ 91 kg; OR 2.73; CI 2.60, 2.87), ≥ 152 cm tall (OR 1.33; CI 1.26, 1.47), diabetic (OR 3.27; CI 2.84, 3.77), multiparous (OR ranged between 1.55 [parity = 1] and 2.15 [parity ≥ 4]), multigravida ≥ 5 (OR 1.99; CI 1.87, 2.11), and women who had high parity for age (OR 1.54; CI 1.40, 1.70), a prior history of an LGA birth (OR 6.65; CI 5.96, 7.41), a stillbirth (OR 1.26; CI 1.08, 1.48), or a neonatal death (OR 1.38; CI 1.13, 1.69). Women who smoked during

Table 4

Crude and Adjusted Odds Ratios (OR) and 95% Confidence Intervals (CI) for Modifiable and Non-modifiable Predictors of Term Large for Gestational Age Births

Characteristic	**Crude OR (95% CI)**	**§Adjusted OR (95% CI)**
Maternal Age (years)		
≤ 17	1.84 (1.70, 1.90)*	1.39 (1.22, 1.58)*
18 – 19	0.74 (0.67, 0.81)*	1.09 (0.99, 1.21)
20 – 29	1.00 Reference	1.00 Reference
30 – 34	1.18 (1.13, 1.22)*	0.98 (0.94, 1.21)
35 – 39	1.28 (1.21, 1.35)*	1.00 (0.94, 1.06)
≥ 40	1.32 (1.17, 1.50)*	0.96 (0.84, 1.09)
Genetic or Constitutional Factors		
Prepregnancy Weight (kg)		
≤ 45	1.07 (0.79, 1.44)	1.19 (0.88, 1.62)
46-90	1.00 Reference	1.00 Reference
≥ 91	2.73 (2.60, 2.87)*	2.52 (2.39, 2.65)*
Height (cm)		
< 152	1.00 Reference	1.00 Reference
≥ 152	1.33 (1.26, 1.47)*	1.30 (1.20, 1.40)*
Lifestyle Factors		
Smoking During Pregnancy		
No	1.00 Reference	1.00 Reference
Yes	0.61 (0.58, 0.64)*	0.58 (0.55, 0.61)*
Alcohol During Pregnancy		
No	1.00 Reference	--
Yes	0.96 (0.75, 1.23)	
Illicit/Street Drug Dependency		
No	1.00 Reference	--
Yes	0.97 (0.55, 1.71)	
Pre-existing Medical Diseases		
Diabetes Mellitus		
No	1.00 Reference	1.00 Reference
Yes	3.27 (2.84, 3.77)*	2.39 (2.09, 2.78)*

(table continues)

Characteristic	Crude OR (95% CI)	[§]Adjusted OR (95% CI)
Obstetrical History		
Parity		
0	1.00 Reference	1.00 Reference
1	1.55 (1.49, 1.62)*	1.43 (1.33, 1.54)*
2	1.72 (1.64, 1.81)*	1.60 (1.48, 1.74)*
3	2.03 (1.89, 2.18)*	1.92 (1.74, 2.12)*
≥ 4	2.15 (1.99, 2.33)*	1.93 (1.66, 2.24)*
High Parity for Maternal Age[†]		
No	1.00 Reference	1.00 Reference
Yes	1.54 (1.40, 1.70)*	1.12 (0.97, 1.28)
Gravidity		
1	1.00 Reference	1.00 Reference
2-4	1.55 (1.48, 1.61)*	1.06 (0.98, 1.14)
≥ 5	1.99 (1.87, 2.11)*	1.11 (1.00, 1.24)
History of LGA birth		
No	1.00 Reference	1.00 Reference
Yes	6.65 (5.96, 7.41)*	4.57 (4.08, 5.12)*
History of stillbirth		
No	1.00 Reference	1.00 Reference
Yes	1.26 (1.08, 1.48)*	0.95 (0.80, 1.12)
History of neonatal death		
No	1.00 Reference	1.00 Reference
Yes	1.38 (1.13, 1.69)*	0.98 (0.80, 1.21)
Medical problems during current pregnancy		
Gestational diabetes mellitus		
No	1.00 Reference	1.00 Reference
Yes	2.07 (1.91, 2.24)*	1.60 (1.47, 1.75)*

(table continues)

Characteristic	Crude OR (95% CI)	§Adjusted OR (95% CI)
Hydramnios (polyhydramnios or oligohydramnios)		
No	1.00 Reference	1.00 Reference
Yes	1.49 (1.30, 1.70)*	1.34 (1.17, 1.54)*
Pregnancy complications		
Pregnancy induced hypertension (PIH)		
No	1.00 Reference	1.00 Reference
Yes	1.35 (1.25, 1.46)*	1.22 (1.13, 1.32)*
Pre-eclampsia/eclampsia		
No	1.00 Reference	–
Yes	1.15 (0.98, 1.36)	
Infant characteristics		
Infant Gender		
Female	1.00 Reference	–
Male	0.98 (0.94, 1.10)	
Gestational age (weeks)		
37	1.00 Reference	–
38	1.01 (0.94, 1.08)	
39	0.92 (0.87, 1.00)	
40	0.95 (0.89, 1.02)	

OR: odds ratio; 95% CI: 95% confidence interval

* Significant $p < 0.001$

§ By controlling all variables in this table

† High parity for age was defined as ≥ 1 birth for mothers ≤ 17 yrs, ≥ previous 3 births for mothers 18-21 yrs, ≥ 4 previous births for mothers 22-24 yrs, ≥ 5 previous births for mothers ≥ 25 yrs

their pregnancy were less likely to have a T-LGA baby (OR 0.61; CI 0.58, 0.64). The odds of delivering a T-LGA infant also increased for women diagnosed with gestational diabetes mellitus (OR 2.07; CI 1.91, 2.24), hydramnios (OR 1.49; CI 1.30, 1.70), and those women who developed PIH (OR 1.35; CI 1.25, 1.46).

Because the risk factors for T-LGA births do not occur independently (e.g., there is an association between maternal obesity and gestational diabetes mellitus), MLR was then used to estimate the independent effects of those maternal, reproductive, and infant characteristics that were significant predictors of T-LGA births, while simultaneously controlling for the effects of the other variables included in the analysis (i.e., potential confounders). Only the significant predictors from the univariable analysis were entered into the MLR analysis. The results of the multivariable modeling for both modifiable and non-modifiable predictors are detailed in Table 4. Adjusted ORs and 95% CI for the study risk factors are presented.

After controlling for potential confounders through MLR, women who were at an increased risk of delivering a T-LGA infant were 17 years of age or younger (OR 1.39; CI 1.22, 1.58), obese (OR 2.52; CI 2.39, 2.65), taller (OR 1.30; CI 1.20, 1.30), diabetic prior to pregnancy (OR 2.39; CI 2.09, 2.78)], multiparous ≥ 3 (OR 1.93; CI 1.66, 2.24), and had previously given birth to an LGA infant (OR 4.57; CI 4.08, 5.12). There was also a statistically significant increased risk of giving birth to a T-LGA infant among women with gestational diabetes (OR 1.60; CI 1.47, 1.75)], hydramnios (OR 1.34; CI 1.17, 1.54), and PIH (OR 1.22; CI 1.13, 1.32). However, there was a negative association between smoking during pregnancy and the incidence of T-LGA births; women were less likely to deliver a T-LGA baby if they smoked during their pregnancy (OR 0.58; CI 0.55, 0.61).

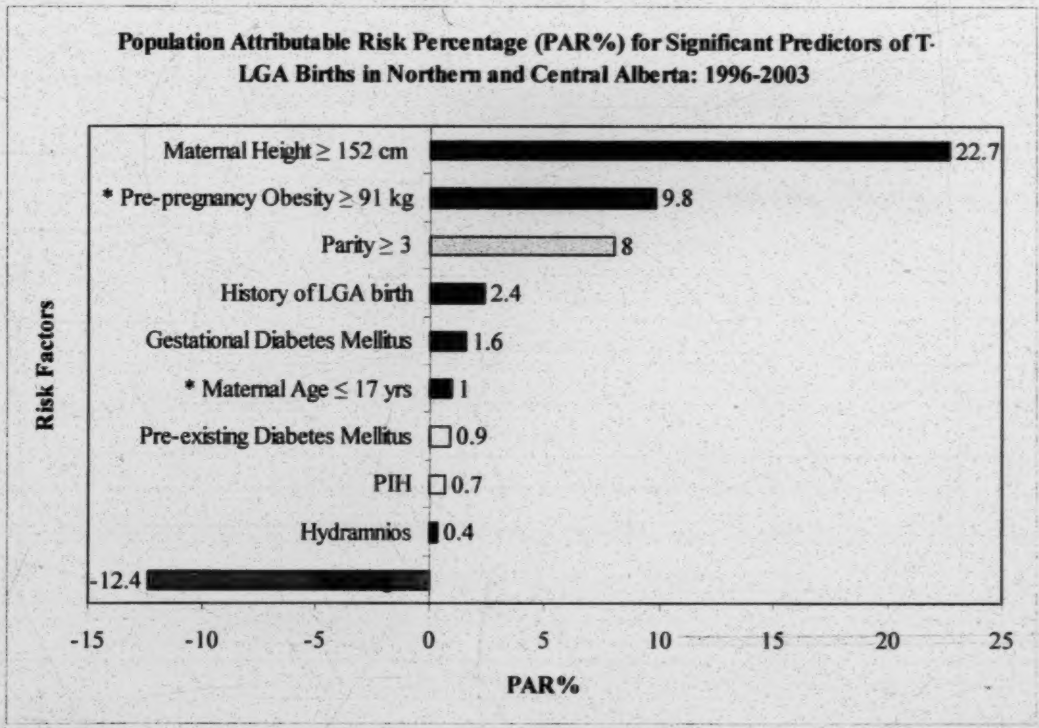
Summary of Major Findings

After adjusting for potential confounders in a MLR analysis, a history of LGA birth was the most powerful predictor of T-LGA births in the index pregnancy; this predictor was associated with a 4.5-fold increase in the likelihood of delivering a T-LGA infant. Women who were obese (prepregnancy weight ≥ 91 kg) and women who had pre-existing diabetes mellitus were 2.5 times more likely to give birth to a T-LGA infant. Compared to nulliparous women, multiparous women with ≥ 3 previous childbirths were twice as likely to have T-LGA births. Maternal age ≤ 17 years, maternal height ≥ 152 cm, gestational diabetes mellitus, hydramnios, and PIH were associated with a slight increase in the odds of delivering a T-LGA birth. Smoking had a protective effect (i.e., women were less likely to deliver a T-LGA baby if they smoked during their pregnancy), and maternal age > 17 years, high parity for maternal age, gravidity, history of stillbirth, or history of neonatal death did not significantly increase a woman's risk of having a T-LGA baby.

Population-Attributable Risk Percentage

The population-attributable risk percentage (PAR%) was calculated for the predictors that remained significant after statistical adjustment for confounders in the risk modeling to determine the potential public health impact of a specific factor; that is, the proportion of T-LGA births that might be eliminated when the risk factor or its effects are removed (Kleinbaum et al., 1982) or minimized through strategic intervention. The PAR% was calculated as follows: $(P_e\,[RR - 1]/1 + P_e\,[RR - 1])*100$, where P_e = proportion exposed in the population and RR = the relative risk that was estimated by the adjusted OR (Kleinbaum et al.). The magnitude of the OR depends on the prevalence of exposure in the population and its associated relative risk. Policy makers and health planners can use this information to determine which population-based interventions may have the greatest influence on reducing the incidence of T-LGA births; intervention(s) would be recommended for conditions with a high PAR (Berkowitz & Lapinski, 1998).

The PAR% associated with significant risk factors for T-LGA births are presented in Figure 3. Only two of the significant predictors are potentially modifiable, both over the short term and the long term: younger maternal age (≤ 17 years old) and prepregnancy weight ≥ 91 kg. Together, younger maternal age and maternal prepregnancy weight ≥ 91 kg contributed to approximately 11% of T-LGA births. Pre-existing medical problems and pregnancy-related conditions and complications (i.e., pre-existing diabetes mellitus, gestational diabetes mellitus, hydramnios, and PIH) were associated with 3.6% of cases of T-LGA births; prior history of LGA birth and multiparity were associated with 10.4% of T-LGA births; and maternal height was associated with 22.7% of T-LGA births. Smoking during pregnancy was a protective risk factor and decreased the likelihood of T-LGA births by 12.4%.



* Modifiable Risk Factors for T-LGA Births

Figure 3. Population-attributable risk percentage (PAR%) for significant predictors of T-LGA births in Northern and Central Alberta: 1996-2003

The results of this analysis have shown that T-LGA births are associated with more non-modifiable risk factors. This finding is consistent with the results of other studies (Jolly et al., 2003; Okun et al., 1997; Rodrigues et al., 2000; Surkan et al., 2004). However, the prevalence or public health importance of other potential modifiable factors that have been identified in other studies such as maternal BMI or maternal weight gain during pregnancy could not be determined in this study; risk factors in this study were limited to potential predictors of T-LGA births contained in the APHP database.

The relationship between 19 maternal study factors and the increased risk of delivering a T-LGA infant was examined in this study. The results show that although several significant risk factors influenced T-LGA births, only a few of these characteristics are modifiable. Moreover, the impact of these risk factors on T-LGA births is modest overall. This suggests that there is an ongoing need for identifying risk factors that are as yet unknown and, in particular, those that are modifiable.

CHAPTER 5:

DISCUSSION

The primary objectives of this study were (a) to determine the prevalence of T-LGA births and secular trends, (b) to identify modifiable and non-modifiable risk factors that increase a woman's risk for delivering a T-LGA infant and their public health importance, (c) to quantify the relative contribution of these risk factors on the incidence of T-LGA births while simultaneously controlling for potential confounders, and (d) to suggest relevant public health strategies for risk reduction and health promotion for childbearing women residing in Northern and Central Alberta.

After adjusting for potential confounders, the risk factors for T-LGA births in this study were younger maternal age ($\leq$ 17 years), increased maternal height ($\geq$ 152 cm), high prepregnancy weight ($\geq$ 91 kg), smoking status, multiparity, previous delivery of an LGA infant, pre-existing diabetes mellitus, gestational diabetes mellitus, hydramnios (polyhydramnios or oligohydramnios), and pregnancy-induced hypertension (PIH). Of the variables that were statistically significant, the strongest predictors of T-LGA births in this study cohort were a previous history of LGA birth and prepregnancy weight $\geq$ 91 kg; these two factors increased the risk of a woman's delivering a T-LGA infant 4.5-fold and 2.5-fold, respectively. Several of these findings have been previously reported in other research studies as being associated with the birth of an LGA infant. In the first section of Chapter 5, the results of this study regarding risk factors will be compared to the findings from other studies that have examined and reported risk factors for LGA births (defined as birth weight > 90th percentile of expected weight for gestational age).

Secular Trends in Large for Gestational Age Birth Rates

In an analysis of all singleton live births without anomalies between 1996 and 2003, this researcher found that the LGA birth rate in Northern and Central Alberta increased significantly from 11.3% to 12.5%. These results were comparable to LGA birth rates reported by other researchers both in Canada and Sweden (Kramer et al., 2002; Surkan et al., 2004; Wen et al., 2003). Using Canadian national birth data for the period between 1978-1979 and 1994-1996, Kramer et al. reported an increase in the proportion of LGA births from 8.0% to 11.5%. Wen et al. also examined secular increases in the rate of LGA births in Canada for a different time period (1981-1997) with a different database. These researchers also reported similar increases in the proportion of LGA births, from 8.0% to 10.0%. The results of this study confirm and extend the works of these researchers that indicate that the LGA birth rates in Canada continue to show increases over time.

Increased rates of LGA births have also been reported internationally. Surkan, Hsieh, Johansson, Dickman, and Cnattingius (2005) observed similar temporal trends for LGA births (defined as birth weight above the 90th percentile of the Swedish fetal growth curve) when they analyzed the Swedish birth data for infants born between 1992 and 2001 (i.e., a relative increase of 10%). However, Yeh and Shelton (2005) found no change in the rate of LGA infants between 1999 and 2003 using USA population-based birth data (i.e., *n* = 70,000 singleton deliveries from a regional perinatal database in western New York). Surkan et al. noted that Yeh and Shelton's data may reflect a systematic change in the birth weight distribution; specifically, that the proportion of infants with birth weights greater than the 97.5 percentile is increasing, whereas that between the 90th and 97.5th percentiles is decreasing.

Overall, the results of this study cohort confirm that the rates of LGA births are continuing to increase over time. Moreover, this overall increase in the rate of LGA births is most likely a result of the increasing numbers of term LGA births in the population. The numbers of preterm and postterm LGA births remained stable over time. These results emphasize the need for continuing surveillance of LGA birth rates both locally and nationally. More research is needed to determine what risk factors are associated with the increasing incidence of high birth weight births in Canada, and the development of population-based prevention programs to decrease risk factor prevalence is essential.

Risk Factors for Term Large for Gestational Age Births

The results of this study indicate that T-LGA births are generally associated with more non-modifiable risk factors: maternal height, pre-existing medical diseases, obstetrical history, medical problems during pregnancy, and pregnancy complications (Table 4). The only modifiable risk factors that were associated with an increased risk of T-LGA births in this study were maternal age 17 years or younger and prepregnancy weight ≥ 91 kg. However, it must be noted that only a partial risk model was developed and that it was limited to the modifiable and non-modifiable risk factors that were contained in the APHP database. The review of the literature revealed a number of other risk factors that should have been included in the study, such as maternal BMI (Jolly et al., 2003), maternal weight gain during pregnancy, ethnicity, and maternal birth weight (Okun et al., 1997), living with the infant's father, and maternal country of birth (Surkan et al., 2004).

Maternal Age

The findings in this study suggest that women in the youngest maternal age group (≤ 17 years) were more likely to deliver a T-LGA infant (OR 1.39; CI 1.22, 1.58); older maternal age was not associated with an increased incidence of T-LGA births. These results are comparable to Surkan et al.'s (2004) findings that younger maternal age (defined as delivery at ≤ 24 years of age) was associated with a slightly increased risk of delivering an LGA baby (OR 1.06; CI 1.01, 1.10) and that there was no maternal age effect on the risk of LGA deliveries among women aged 30 years or older. Other researchers have also reported an association between younger maternal age and an increased rate of LGA infants. Using UK birth data, Jolly et al. (2003) reported that younger women (maternal age < 18 years) were at an increased risk for LGA births (OR 1.19; CI 1.01, 1.40). However, in a Canadian study of non-diabetic women, Okun et al. (1997) found no maternal age effect for LGA births; whether or not these researchers would have found a similar association between younger maternal age and LGA births if they had not excluded diabetic women from their study sample is unknown.

Although one previous study reported an association between older maternal age and high birth weight deliveries, there was no association between older maternal age and the delivery of a T-LGA birth in this study. In the UK, Jolly et al. (2003) reported a slight increase in the risk of LGA births among older women between 35 and 40 years of age (OR 1.14; CI 1.08, 1.19) and women over 40 years old (OR 1.22; CI 1.11, 1.35). According to these researchers, the higher growth velocity may be attributable to age-related changes in maternal metabolism in these older women; however, their finding was not duplicated in this study.

In this study maternal age may have also indirectly affected T-LGA births through its influence on other risk factors. The increasing prevalence of overweight and obesity in children and adolescents globally (Dietz, 2004; Surkan et al., 2004) may place younger mothers at greater risk for T-LGA births; obese mothers are more likely to deliver heavy infants (Bergmann et al., 2003). It could also be hypothesized that perhaps older women are delivered at an earlier gestation (e.g., because of underlying medical conditions such as diabetes mellitus), thereby reducing the likelihood of achieving a higher birth weight infant (Jolly et al., 2003). Moreover, older women may be more likely to develop problems during pregnancy or pregnancy complications, resulting in preterm births or shortened gestational durations and correspondingly smaller babies. Therefore, older women are possibly less likely to have T-LGA births.

Genetic and Constitutional Factors

Prepregnancy Weight

In this study prepregnancy weight ≥ 91 kg was associated with a 2.5-fold increase in a woman's chances of delivering a T-LGA infant. This is in general agreement with the findings reported in previous studies (Jolly et al., 2003; Okun et al., 1997; Rodrigues et al., 2000). The association between high maternal weight and its impact on fetal weight has been well documented: Obesity reduces insulin sensitivity and increases the availability of accessible glucose for maternal-fetal transport, causing increases in intrauterine growth (Langer, 2000). Okun et al. found that the risk of delivering an LGA baby increased 1.56 for every 7 kg increase in maternal weight before pregnancy.

Similarly, Rodrigues et al. reported that for every 5 kg of maternal weight gained prior to pregnancy, the risk of an LGA delivery among Cree infants compared to non-Native infants increased by 1.15 and 1.22, respectively. Researchers have also reported that women with a high BMI (> 25 kg/m^2) have an increased risk of delivering an LGA infant (Jolly et al.; Surkan et al., 2004).

Maternal Height

Taller stature (≥ 152 cm) was positively associated with an increased incidence of T-LGA births (OR 1.30; CI 1.20, 1.40) in this study, although heavy babies might be considered normal for tall women in some countries (Bergmann et al., 2003). Other researchers have previously reported similar results; however, the definitions of what constitutes taller stature have varied across the different studies (Okun et al., 1997; Rodrigues et al., 2000; Surkan et al., 2004). A group of Canadian researchers found that the risk of delivering an LGA baby increased by 1.3 for every 7 cm increase in maternal height (Okun et al.). Similarly, Rodrigues et al. reported that for every 5 cm increase in maternal height, the risk of an LGA delivery among Cree infants increased by 1.48. In Sweden, investigators also found a positive association between maternal stature (≥ 170 cm tall) and the risk of delivering an LGA infant (OR 1.86; CI 1.81, 1.91; Surkan et al.). However, because of the large sample size and the extremely high prevalence of women ≥ 152 cm tall in this study (96%), it is probable that the association with maternal height is statistically significant but not clinically relevant. It is also conceivable that the taller stature of women with T-LGA births can be merely construed as a secular trend of no particular relevance to health (Bergmann et al.).

Lifestyle Factors

Smoking

It has been firmly established that the smoking status of pregnant women has a significant and direct impact on infant birth weight. In this study one quarter (24.5%) of the women smoked during their pregnancy. The results show that women who smoked were less likely to deliver a T-LGA baby (OR 0.58; CI 0.55, 0.61). Specifically, smoking during pregnancy had a protective effect in the incidence of T-LGA births. Other studies have also reported similar findings (Jolly et al., 2003; Okun et al., 1997; Rodrigues et al., 2000; Surkan et al., 2004). In Canada, Rodrigues et al. reported a protective effect in non-Native women who smoked (OR 0.51; CI 0.39, 0.66), and Okun et al. found a protective effect in pregnant women who smoked 5 cigarettes per day (OR 0.66; CI 0.56, 0.78). Surkan et al. examined data in Sweden and also reported that pregnant women who smoked had a reduced risk of delivering an LGA infant, and the risk was directly proportionate to the number of cigarettes smoked daily; that is, OR 0.52 (CI 0.49, 0.55) for women who smoked between 1 and 9 cigarettes per day, and OR 0.39 (CI 0.36, 0.41) for women who smoked 10 or more cigarettes per day. In the UK, Jolly et al. also found that smoking had a protective effect (OR 0.54; CI 0.52, 0.57) in LGA births.

Pre-existing Medical Diseases

Diabetes Mellitus

The results of this study indicate that women with pre-existing diabetes mellitus were 2.4 times more likely to deliver a T-LGA infant. The increased risk in this study was lower than the risk estimates reported in a British study that Jolly et al. (2003) conducted; these researchers reported that the risk of delivering an LGA infant increased sevenfold for diabetic women (OR 6.97; CI 5.96, 8.16). The differences in risk estimates may be due to the differences in the sample used. In other studies that examined risk-factor epidemiology for LGA births, diabetic women may have been excluded because the effects of diabetes mellitus on high birth weight deliveries were already well described (Berard et al., 1998; Boyd et al., 1983; Lapunzina et al., 2002; Spellacy et al., 1985), and the researchers wanted to examine the effects of other risk factors in non-diabetic populations. For instance, Okun et al. (1997) excluded women from their study who had pre-existing medical conditions that were known to have an effect on fetal growth, such as diabetes mellitus. Rodrigues et al. (2000) also excluded women with pre-gestational diabetes mellitus from their study. Therefore, lack of information may also be influenced by the specific study questions being asked as well as the exclusion criteria used in the studies.

Obstetrical History

Parity

The findings in this study are in general agreement with those of several others that have found a positive association between multiparity and LGA births (Jolly et al., 2003; Okun et al., 1997; Surkan et al., 2004). In this study increasing parity was associated with higher odds of T-LGA births, and the chances were highest among women with ≥ 3 previous childbirths, where there was a twofold increased risk. Similarly, Jolly et al. reported a twofold increased risk when parity exceeded four (OR 2.20; CI 2.02, 2.40). Other investigators reported that when parity increased from two to greater than five, the risk of an LGA birth increased from 2.2 to 3.2 (Surkan et al.).

Prior Obstetrical History

The results of this study showed that a previous history of delivering an LGA neonate was the strongest predictor of T-LGA births in the current pregnancy; women who had delivered an LGA infant in a previous pregnancy experienced a 4.5-fold increased risk of delivering an LGA infant in subsequent pregnancies. It is conceivable that women who already delivered an LGA infant may be at an increased risk of another LGA birth as a result of the persistence of the same type of maternal genetic, constitutional, and/or metabolic features (Okun et al., 1997; Rodrigues, Teles, & Barros, 1999). Findings for this risk factor were not included in other studies in the literature reviewed.

Medical Problems During the Current Pregnancy

Gestational Diabetes Mellitus

Gestational diabetes mellitus was a significant predictor for T-LGA births in this study (OR 1.60; CI 1.47, 1.75). This positive association between gestational diabetes mellitus and LGA births is consistent with the findings of previous studies (Jolly et al., 2003; Surkan et al., 2004). However, the risk estimate for the effect of gestational diabetes on the incidence of LGA births in these studies was approximately two times higher than the risk estimated in the study conducted by this researcher. It is possible that the differences in risk estimates may be a result of differences in the study sample. In the UK, Jolly et al. reported a nearly three-fold increase in the risk of LGA births in women with gestational diabetes mellitus (OR 2.77; CI 2.51, 3.07). Similarly, Surkan et al. found a 3.4-fold increased risk of LGA births in Swedish women with gestational diabetes mellitus (OR 3.35; CI 3.06, 3.63).

Hydramnios

Women in this study who had hydramnios (polyhydramnios or oligohydramnios) were 1.3 times more likely to deliver a T-LGA neonate (CI 1.17, 1.54). Because polyhydramnios and oligohydramnios were aggregated into one category, their independent effects on T-LGA births cannot be estimated. Moreover, the increase in odds is slight, and this characteristic was not previously examined in other studies included in the literature review for confirmation or comparison. It is also necessary to examine these two types of hydramnios separately in future studies to determine whether they have an independent and significant effect on the increased incidence of LGA births.

Pregnancy Complications

Pregnancy-Induced Hypertension (PIH)

In this study PIH was associated with a slight increase in the likelihood of T-LGA births (OR 1.22; CI 1.13, 1.32). Other researchers have also shown a positive association between gestational hypertension and the risk of delivering a LGA infant (Xiong, Demianczuk, Buekens, & Duncan Saunders, 2000). In a retrospective cohort study of *n* = 97,270 pregnancies delivered between 1991 and 1996 in Northern and Central Alberta, Xiong et al. found that, after adjustment for potential confounders, the risk of delivering an LGA infant was higher for women with gestational hypertension (OR=1.50; CI 1.22, 1.85). These results were consistent with the findings in a population-based study conducted in China (*n* = 16,936 pregnancies) in 1989-1990 (Xiong et al., 1999). The researchers suggested that some patients may deliver larger infants because of a growth-enhancing effect of high blood pressure that protects against the decreased uteroplacental perfusion (Xiong et al., 2000). PIH was not evaluated in other epidemiologic studies included in the literature review.

Pre-eclampsia

There was no association between pre-eclampsia and T-LGA births in this study, possibly because of the relatively small proportion of pre-eclamptic women (1.1%). Researchers in the UK who examined this risk factor also did not report an association between pre-eclampsia and LGA births (Jolly et al., 2003). However, Surkan et al. (2004) reported that Swedish women diagnosed with pre-eclampsia had a slightly increased risk of LGA births (OR 1.17; CI 1.08, 1.26). In a study that examined the effect of gestational hypertension and pre-eclampsia on fetal growth between 1991 and 1996 ($n = 97{,}270$), Xiong et al. (2000) also found a positive association between pre-eclampsia and LGA births (OR 1.87; CI 1.31, 2.67). The researchers suggested that these women possibly deliver larger infants because pre-eclampsia usually occurs later in pregnancy, so the decreased uteroplacental perfusion may be too short in duration to cancel the earlier growth-enhancing effects of increased blood flow caused by higher blood pressure. Moreover, other study findings also suggest that uteroplacental blood flow may be normal or increased in the majority of pre-eclamptic women secondary to increased maternal cardiac output (Xiong, Demianczuk, Duncan Saunders, Wang, & Fraser, 2002). The pre-eclampsia effect may also be dependent on other clinical characteristics of the women who participated in the studies, such as maternal obesity, diabetes mellitus, and smoking; however, these researchers excluded or controlled for potential confounders in their analysis (Surkan et al., Xiong et al. 2000; Xiong et al. 2002).

Infant Characteristics

The null findings for infant gender and gestational age on T-LGA births in this study are supported by findings from previous studies of LGA births (Okun et al., 1997; Rodrigues et al., 2000; Surkan et al., 2004). In a Canadian study that Okun et al. conducted, researchers found no association between infant gender and the risk of delivering an LGA infant. Similarly, gestational age did not have an effect on LGA births in their study (Okun et al.). Rodrigues et al. also did not report a gestational age effect on LGA births; these researchers did not examine the effect of infant gender on LGA births. Using Swedish data, Surkan et al. also found no gestational age effect on LGA births, and they did not examine the effect of infant gender in their study.

Study Strengths and Limitations

The primary objective of this study was to determine the etiology of T-LGA births in Northern and Central Alberta residents, and to determine where and to what extent T-LGA births could be prevented in this population. A population-based, retrospective cohort study using a case-control design was used to address these study questions. Because of the large birth cohort included in this study (*n* = 115,198), there was sufficient study power to examine numerous potential etiologic factor and covariates, as well as interactions among the factors. By comparing women with T-LGA births (cases) and women with T-AGA births (controls), it was feasible to explore the potential impact of maternal age, genetic and constitutional factors, lifestyle factors, pre-existing medical diseases, obstetrical history, medical conditions during pregnancy, pregnancy complications, and infant characteristics on the increased incidence of T-LGA births in a geographically defined population.

Several features of this study design increased the validity of the study results. Because it was a geographically defined population-based study that included all eligible births in Northern and Central Alberta that met the study inclusion criteria, the potential problem of selection bias was minimized. The large sample size resulted in sufficient study power to examine several maternal and infant characteristics or exposures simultaneously as possible risk factors for T-LGA births, and the stepwise MLR adjusted for potential confounders. However, the large sample size can also be considered a limitation: It can be expected that group differences could result in statistically significant differences that may not be clinically important. However, this limitation did not affect the validity of the study conclusions; the results of previous studies confirmed the findings reported in this study.

The pregnancy and birth data used in this study for modeling the risks of T-LGA births were contained in a well-validated computerized database, and potential confounders were controlled for in the risk modeling. Recall bias was minimized because most of the data are recorded before pregnancy outcomes are known. The Provincial Delivery Record (Parts 1 and 2) are completed within the first 24 hours of birth, but the assessment of potential maternal risk factors would have been completed prior to the birth. Therefore, the birth outcome should not have influenced the accuracy of the exposures reported in this study (i.e., prevention of response bias). The APHP perinatal administrative database that was used in this study contained maternal, reproductive, and infant data on all hospital deliveries in Northern and Central Alberta; however, deliveries occurring outside of hospitals were not included. These births constituted a small proportion of the total number of births used in the analysis, and therefore it is assumed that the results of the study would not have changed if data on these deliveries had been captured in the database and included in the risk modeling.

One of the limitations of this study is the finite set of risk factors that were available in the APHP perinatal database for risk modeling. From the review of the literature, a number of relevant factors were associated with the risk of delivering an LGA infant that were not contained in this database and consequently were not included in the risk modeling. These risk factors included ethnicity, maternal BMI, maternal weight gain during pregnancy, living with the infant's father, maternal birth weight, and maternal country of origin. Therefore, only a partial risk model for T-LGA births could be developed in this study.

Another limitation of the database used in this study was the way in which specific variables were defined and aggregated in the APHP database. For example, instead of entering maternal height and weight as continuous variables, risk categories were defined arbitrarily, and women were classified into two groups: height (< 152 cm vs. ≥ 152 cm) and weight (< 45 kg; 46-90 kg, and ≥ 91 kg), respectively. This restricted the capacity to examine the combined effects of a woman's height and weight; specifically, the effect of BMI on the risk of delivering an LGA infant, which is a useful measure in determining obesity and is a more accurate way to determine when extra weight is likely to increase health risks. Similarly, the risk associated with lifestyle factors such as the use of cigarettes, alcohol, and street drugs during pregnancy may be better evaluated as continuous variables to determine the increased risk associated with different levels of exposure (e.g., risk estimated as a function of the number of cigarettes smoked or the amount and type of alcohol consumed or drugs used) and changes in exposure over the course of the pregnancy.

Another possible limitation may be misclassification of exposure to lifestyle factors, and reporting bias; for example, underreporting of smoking, alcohol, and drug use. In another example, *hydramnios* is classified as a risk factor that includes both polyhydramnios and oligohydramnios; it is not possible to distinguish which one of the two conditions is actually present. However, these factors may impact differently on fetal growth and confound the results of the risk modeling used in this study. Because it was possible to develop only a partial risk model in this study, additional study is required because the findings from this study might have been different with the addition of other risk factors and covariates.

Secondary data analysis was used in this study, and this was also considered a possible limitation in this observational study. Although there is a rigorous data validation process in place, inherent miscoding and/or misclassification problems and lack of precision in reported diagnoses of medical problems and morbidities in the database are still possible. Moreover, the data were collected by multiple personnel, thus increasing the potential for random error.

This study population is limited to women in Northern and Central Alberta who gave birth to a singleton liveborn infant with no major anomalies, so the results of this study can be generalized only to women who delivered a singleton liveborn infant with no major anomalies. Moreover, it is not possible to determine whether any of the predictors identified in the study "caused" T-LGA births; the logistic regression could only describe the relationship between various risk factors and the birth outcome. Instead, it can only be stated that these factors were associated with the birth outcome; that is, T-LGA births.

A final limitation of this study is related to the use of logistic regression to develop the hypothetical risk model for T-LGA births. This analytic technique requires that the observations be independent. However, within the eight-year study period, it is conceivable that a certain proportion of the study sample may have given birth more than once and that some of the observations would no longer be independent. Given that anonymous administrative data is used in this study, it is not possible to identify and eliminate those women for whom multiple observations were recorded.

Implications of the Study Findings

The prevention of T-LGA births is challenging because these deliveries are not restricted to a unique group of women with distinctive characteristics. Moreover, there are multiple risk factors, and prevention strategies cannot be limited to a single intervention to be implemented by an exclusive care provider. The collaborative efforts of interdisciplinary healthcare providers is essential to develop and sustain programs that endorse antenatal health promotion and risk reduction strategies for T-LGA births, with reinforcement during pregnancy and after delivery.

The most important predictors of T-LGA births in this study were prepregnancy weight ≥ 91 kg, younger maternal age, maternal height, non-smoking, previous history of an LGA birth, high parity, pre-existing diabetes mellitus, gestational diabetes mellitus, hydramnios, and PIH. Using this information, nurses and other healthcare personnel can provide pre-conception counseling and endorse specific risk reduction strategies that advocate maintaining optimal physical health and fitness before entering pregnancy and adequate nutritional intake and exercise levels during pregnancy and after delivery. In addition, prenatal care and antenatal surveillance are important to recognize, treat, and/or control existing medical diseases such as diabetes mellitus and medical conditions that develop during pregnancy such as gestational diabetes mellitus, and pregnancy complications such as PIH.

Prepregnancy weight ≥ 91 kg was the most significant modifiable predictor for T-LGA births in this study. Effective upstream population-based nursing interventions include pre-conception counseling with education about possible maternal and fetal risks of obesity during pregnancy, physical fitness, and dietary control; and encouragement of obese women to participate in a weight reduction program before attempting pregnancy (American College of Obstetricians & Gynecologists, 2005; Okun et al., 1997; Orskou et al., 2003; Surkan et al., 2004). Moreover, nurses can collaborate with other community partners (e.g., nutritionists, weight loss specialists, physical fitness instructors) to facilitate long-term nutrition counseling that integrates healthy food choices that influence selection when grocery shopping and eating in restaurants or fast-food establishments. Nurses in the community can also encourage and facilitate participation in physical fitness programs to help women to manage their weight appropriately. Findings from previous studies have shown that even moderate physical activity reduces the risk for T-LGA births (Alderman, Zhao, Holt, Watts, & Beresford, 1998). Secondary prevention strategies for obese women who are already pregnant include continuation of nutrition counseling and exercise programs after delivery, and consultation with nutritionists and/or weight loss specialists before attempting future pregnancies.

Although several etiological factors (modifiable and non-modifiable) for T-LGA births were identified in this study, prepregnancy weight ≥ 91 kg is likely to be the most relevant risk factor for health care decision makers and policy planners. The PAR% calculations for this study show that approximately 10% of T-LGA births might be eliminated if prepregnancy weight ≥ 91 kg could be reduced or avoided. Within the constraints of limited financial and professional health care resources, population-based health promotion activities and important secondary and tertiary prevention programs that target prepregnancy weight ≥ 91 kg in Northern and Central Alberta would have the greatest impact on the prevention of T-LGA births in these women. Moreover, T-LGA births have also been linked to long-term sequelae including obesity, hypertension, and type II diabetes mellitus (Boney et al., 2005; Pettitt & Knowler, 1998), and obese women are more likely to deliver LGA infants (Bergmann et al., 2003). It is possible that preventing or reducing prepregnancy obesity can potentially interrupt this "snowball effect" of T-LGA births and lessen the likelihood of developing obesity-related health issues later in life.

Nurses and other health leaders can assist by lobbying health care planners and policy makers for adequate funding to develop and implement interventions that address the etiology of T-LGA births and inform women of the risks factors and adverse events associated with T-LGA births before they become pregnant, as well as provide support during pregnancy and after delivery. These include delivering educational information through conventional and unconventional means (e.g., media advertisements, or pre-conception counseling, prenatal classes, and postnatal sessions), as well as providing human and financial resources to support risk reduction and health promotion strategies (e.g., professional and support staff, covering of transportation expenses to bring clients to information sessions, provision of meeting space, and supplementation of advertising costs). Subsidized physical fitness programs in conjunction with access to nutrition counselors would also be useful to endorse and sustain healthy lifestyles and reduce or minimize obesity. Therefore, this issue needs to remain on the social, political, educational, and health agenda of health care planners and policy makers to ensure that adequate resources are made available to support and sustain suitable intervention programs.

The findings in this study also show an increased risk for T-LGA births in women of younger maternal age (≤ 17 years). There is an increased need for counseling to prevent teenage pregnancies, and those teenagers who become pregnant must receive information tailored to their medical, social, nutritional, and educational requirements. This group is also at risk for poor pregnancy outcomes because of their limited knowledge or understanding of sex, reproductive health, and its consequences (Leishman, 2004). However, the existing social structure of the community may not address the needs and critical concerns of these pregnant adolescents adequately. It is possible that more accessible and appropriate care may be provided by outreach programs and multidisciplinary teams that are sensitive to the needs of teens (Stewart et al., 1996). These include physiological as well as psychological concerns such as parenting issues, poor birth outcomes, sexually transmitted diseases, abortion, poor self-esteem, fragmented social relationships, attention-seeking behaviors, peer pressure, and suicide (Leishman).

Through collaborative partnerships among health care, education, and other community partners (such as public advertising agencies), nurses can strengthen and/or deliver educational messages regarding pre-conception counseling that target these vulnerable adolescents through, for example, music, television programs, billboards, and advertisements on buses used for public transportation; or they can access this at-risk population wherever they congregate, such as in schools, malls, and clubs. Essential elements of these educational programs must include health counseling, the facilitation of peer support, home visits, and trips to schools and/or other locations that are socially appropriate for this age group. Because nurses focus on the broader issues that influence health, they are ideally placed to work with community partners to develop and implement strategies that address the specific needs of these younger childbearing women.

The importance of also identifying non-modifiable risk factors for T-LGA births is relevant for secondary and tertiary prevention initiatives that can be utilized in pre-conception counseling and/or prenatal care to facilitate optimal health outcomes for the mother and her infant through antenatal surveillance, screening, prompt identification of problems, and timely medical management. It is essential that care providers be aware of these risk factors so that they can facilitate appropriate screening and conduct surveillance for early identification and management of at-risk pregnancies; awareness also enables them to educate the community about the potential risk factors and facilitate access to treatment for medical conditions and pregnancy complications as required. Informal or unconventional means of communication such as the use of advertising in public transportation and supermarkets as well as on billboards, television, and community publications such as newsletters or flyers can help to dispense information further, more quickly, and easily (White, 2004).

Future Recommendations

The findings of this study are limited because only a partial risk model for T-LGA births could be developed. Therefore, it is necessary to conduct further research and future risk modeling that includes other previously identified risk factors and covariates that also have an impact on fetal growth and birth weight to extend our understanding of potential predictors and their impact on LGA births. Other factors that should be included in the APHP database and in subsequent risk models to determine their independent effects on LGA births are maternal weight gain during pregnancy, maternal birth weight, maternal BMI, living with the infant's father, ethnicity, and country of origin.

Although the adverse effect of nutritional disorders on pregnancy outcome is well recognized, there is no consensus on the role of maternal anthropometric measures as a guide for pregnancy surveillance or the ideal weight gain for a healthy pregnancy (Rodrigues et al., 1999). Whether the effect of nutritional control on prepregnancy weight gain may have other undesirable outcomes is also unknown. Moreover, it has been hypothesized that increased birth weight and increased BMI in adulthood are linked and that maternal birth weight might be predictive of the infant's birth weight, so that increased birth weight might not be entirely influenced by maternal BMI but may be determined in part at the time of the mother's birth (Surkan et al., 2004). Further prenatal surveillance and research investigations in these areas, including longitudinal studies that assess health status from conception through adulthood, could provide useful information for future consideration.

A comprehensive provincial perinatal surveillance system of risk factors that affect pregnancy outcomes would help to improve perinatal health surveillance research in Alberta immensely (White, 2004). It is important for practitioners and database managers to continue to work collaboratively to ensure that regional and provincial databases in Alberta are capable of supporting perinatal health surveillance research appropriately. Although an inclusive database is important, its success relies upon meticulous attention to the data that are revealed from the full completion of the forms that support the database. For example, $n = 2,652$ eligible mother-infant pairs were excluded from the analysis in this study because of the missing values for gestational age, infant birth weight, and infant gender that were required for classification of the birth outcome according to the national reference standards for LGA births. Moreover, up to 2.3% of the information was missing for some of the risk factors that were examined in this study. This issue becomes the responsibility of all practicing health professionals, including nurses. It is also essential that regional and provincial surveillance systems correspond to the Canadian Perinatal Surveillance System so that national comparisons of trends are also possible. Therefore, multiple stakeholders across numerous sectors must take collective action to ensure that appropriate antenatal surveillance remains on the educational, social, political, and health agendas of local, provincial, and national governments (White, 2004).

Nurse researchers can lobby those who are responsible for revising provincial databases to include the risk factors for LGA births that were identified in the literature review but are not currently included in the APHP database (e.g., ethnicity, living with the infant's father, prepregnancy BMI, maternal weight gain during pregnancy, and maternal birth weight). It would also be useful to extend the current data collection process for existing variables such as genetic and constitutional factors (i.e., recording as continuous instead of categorical variables), and lifestyle factors (i.e., documenting the actual number of cigarettes and the amount and type of alcohol consumed or street drugs used). Polyhydramnios and oligohydramnios must be reported as separate conditions. Information on socioeconomic status and level of physical activity could also be useful in future prenatal surveillance studies. It is necessary to include these expanded elements in the prenatal surveillance database to develop a more comprehensive etiological model and extend our understanding of modifiable and non-modifiable risk factors that are associated with T-LGA births. Ultimately, it may be most prudent to focus research efforts on modifiable risk factors for T-LGA births.

Finally, anthropometric variables have an important role in determining infant birth weight. Jolly et al. (2003) suggested the use of more sophisticated means of assessing relative birthweight such as the individualized birth weight ratio where the influences of maternal height, weight gain in early pregnancy, ethnicity, parity, and infant gender controlling for gestational age are considered. Other researchers recommended the ponderal index, or the birth symmetry index, as potential alternative measurements (Berard et al., 1998). The ponderal index is the ratio between 100 times the weight and the cube of the length of an infant; it is reasonably free of influences from race, gender, and gestational age. The birth symmetry index is defined as the ratio between weight and length, each divided by the weight and length, respectively, at the 50th percentile. Although cumbersome to calculate, these indices may provide a more standardized measurement of birth weight data across different populations.

Conclusions

The secular trend analysis reported in this study confirms that LGA rates are continuing to increase over time. These LGA births are associated with several maternal complications (such as cephalopelvic disproportion, increased or prolonged and obstructed labor, genital tract injury including third- and fourth-degree perineal tears, anal sphincter rupture, pudendal nerve damage, instrument and caesarean section deliveries, and postpartum hemorrhage) and adverse neonatal outcomes (such as shoulder dystocia, brachial or facial nerve injuries, skeletal injuries including clavicular or humerus fractures, birth asphyxia, stillbirth, and neonatal hypoglycemia). Long-term sequelae include cancer (in children and adults), metabolic syndrome, obesity, and non–insulin-dependent (type II) diabetes.

The results of this study indicate that the main predictors of T-LGA births are a previous history of an LGA delivery, prepregnancy weight ≥ 91 kg, pre-existing diabetes mellitus, gestational diabetes mellitus, parity ≥ 3, and younger maternal age ≤ 17 years. However, the indicators for a lifestyle that promotes prepregnancy weight ≥ 91 kg may have the greatest modifiable effect on the prevalence of T-LGA births.

The population-attributable risk estimates for the significant risk factors reported in this study indicate that approximately 10% of T-LGA births might be eliminated if prepregnancy weight ≥ 91 kg could be minimized or prevented. Therefore, a population-based intervention that focuses on normalizing prepregnancy weight and decreasing the incidence of maternal obesity is warranted (Okun et al., 1997). Ultimately, risk reduction and health promotion strategies to normalize prepregnancy weight might be most effective in reducing the overall incidence of T-LGA births, making prevention of prepregnancy obesity a public health priority.

REFERENCES

Aerts, L., & Van Assche, F. A. (2003). Intra-uterine transmission of disease. *Placenta, 24*(10), 905-911.

Alberta Health and Wellness. (1999). *A report on the health of Albertans*. Edmonton, AB: Alberta Health.

Alberta Health and Wellness. (2004). Reproductive Health Working Group. Birth weight: Large for gestational age and high birth weight. In *Alberta reproductive health: Pregnancies and births*. Edmonton, AB: Author.

Alderman, B. W., Zhao, H., Holt, V. L., Watts, D. H., & Beresford, S. A. (1998). Maternal physical activity in pregnancy and infant size for gestational age. *Annals of Epidemiology, 8*(8), 513-519.

Alsunnari, S., Berger, H., Sermer, M., Seaward, G., Kelly, E., & Farine, D. (2005). Obstetric outcome of extreme macrosomia. *Journal of Obstetrics & Gynaecology Canada, 27*(4), 323-328.

American College of Obstetricians and Gynecologists. (2000, November). *Fetal macrosomia* (ACOG Practice Bulletin No. 22.) Washington, DC: American College of Obstetricians and Gynecologists (ACOG).

American College of Obstetricians and Gynecologists. (2005). Obesity in pregnancy: ACOG Committee Opinion No. 315. *Obstetrics and Gynecology, 106*(3), 671-675.

Ananth, C. V., & Wen, S.W. (2002). Trends in fetal growth among singleton gestations in the United States and Canada, 1985 through 1998. *Seminars in Perinatology, 26*(4), 260-267.

Armstrong, I. E., Robinson, E. J., & Gray-Donald, K. (1998). Prevalence of low and high birthweight among the James Bay Cree of Northern Quebec. *Canadian Journal of Public Health, 89*(6), 419-420.

Axelsson, O. (1990). Delivery of the large fetus. *Acta Obstetrics and Gynecology Scandinavia, 69*, 473-474.

Barker, D. J. P. (Ed.). (1992). *Fetal and infant origin of adult disease*. London: BMJ.

Berard, J., Dufour, P., Vinatier, D., Subtil, D., Vanderstichele, S., Monnier, J. C., et al. (1998). Fetal macrosomia: risk factors and outcome. A study of the outcome concerning 100 cases > 4500 g. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 77*, 51-59.

Bergmann, R., Richter, R., Bergmann K., Plagemann, A., Brauer, M., & Dudenhausen, J. W. (2003). Secular trends in neonatal macrosomia in Berlin: Influences of potential determinants. *Pediatric and Perinatal Epidemiology, 17,* 244-249.

Berkowitz, G. S., & Lapinski, R. H. (1998). The relative and attributable risk estimates for birth. *Prenatal Neonatal Medicine, 3*, 53-55.

Boney, C. M., Verma, A., Tucker, B. S., & Vohr, B. R. (2005). Metabolic syndrome in childhood: Association with birth weight, maternal obesity, and gestational diabetes mellitus. *Pediatrics, 115*(3), e290-e296.

Bonnellie, S. R., & Raab, G. M. (1997). Why are babies getting heavier? Comparison of Scottish births from 1980 to 1992. *British Medical Journal, 315*(7117), 1205.

Boulet, S. L., Alexander, G. R., Salihu, H. M., & Pass, M. (2003). Macrosomic births in the United States: Determinants, outcomes, and proposed grades of risk. *American Journal of Obstetrics and Gynecology, 188*(5), 1372-1378.

Boyd, M. E., Usher, R. H., & McLean, F. H. (1983). Fetal macrosomia: Prediction, risks, proposed management. *Obstetrics and Gynecology, 61*(6), 715-722.

Brunt, J. H., & Shields, L. E. (2000). Epidemiology in community health nursing: Principles and applications for primary health care. In M. J. Stewart (Ed.), *Community nursing: Promoting Canadians' health* (2nd ed., pp. 564-583). Toronto, ON: W.B. Saunders.

Bryant, D. R., Leonardi, M. R., Landwehr, J. B., & Bottoms, S. F. (1998). Limited usefulness of fetal weight in predicting neonatal brachial plexus injury. *American Journal of Obstetrics and Gynecology, 179*, 686–689.

Butterfield, P. (2002). Upstream reflections on environmental health: An abbreviated history and framework for action. *Advances in Nursing Science, 25*(1), 32-49.

Dietz, W. H. (2004). Overweight in childhood and adolescence. *The New England Journal of Medicine, 350*(9), 855-857.

Dor, N., Mosberg, H., Stern, W., Jagani, N., & Schulman, H. (1984). Complications in fetal macrosomia. *New York State Journal of Medicine,* 302-305.

Dyck, R. F., & Tan, L. (1995). Differences in high birthweight rates between Northern and Southern Saskatchewan: Implications for Aboriginal peoples. *Chronic Diseases in Canada, 16*(3), 107-110.

Evers, I. M., de Valk, H. W., Mol, B. W., ter Braak, E. W., & Visser, G. H. (2002). Macrosomia despite good glycaemic control in Type 1 diabetic pregnancy: Results of a nationwide study in the Netherlands. *Diabetologia, 45,* 1484-1489.

Ferber, A. (2000). Maternal complications of fetal macrosomia. *Clinical Obstetrics and Gynecology, 43(2),* 335-339.

Gregory, K. D., Henry, O. A., Ramicone, E., Chan, L. S., & Platt, L. S. (1998). Maternal and infant complications in high and normal weight infants by method of delivery. *Obstetrics and Gynecology, 92*(4), 507-513.

Haram, K., Pirhonen, J., & Bergsjø, P. (2002). Suspected big baby: A difficult clinical problem in obstetrics. *Acta Obstetrics and Gynecology Scandinavia, 81*(3), 185-194.

Health Canada. (2002). *Towards a common understanding: Clarifying the core concepts of Population Health: A Health Canada discussion paper*. Retrieved April 15, 2005, from http://www.phac-aspc.g.ca/ph-sp/phdd/approach/ approach.htm.#health

Jolly, M., Sebire, N., Harris, J., Regan, L., & Robinson, S. (2003). Risk factors for macrosomia and its clinical consequences: A study of 350,311 pregnancies. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 111,* 9-14.

Kleinbaum, D. G., Kupper, L., & Morgenstern, H. (1982). *Epidemiologic research.* Belmont, CA: Lifetime Learning.

Kramer, M. S. (1987). Intrauterine growth and gestational duration determinants. *Pediatrics, 80,* 502-511.

Kramer, M. S., Morin, I., Yang, H., Platt, R., Usher, R., McNamara, H., et al. (2002). Why are babies getting bigger? Temporal trends in fetal growth and its determinants. *Journal of Pediatrics, 141,* 538-542.

Kramer, M. S., Platt, R. W., Wen, S. W., Joseph, K. S., Allen, A., Abrahamowicz, M., et al. (2001). A new and improved population-based Canadian reference for birth weight for gestational age. *Pediatrics 108*(2). Retrieved January 9, 2005, from http://www.pediatrics.org/cgi/content/full/108/2/e35

Kramer, M. S., Platt, R., Yang, H., Joseph, K., Wen, S., Morin, L., et al. (1998). Secular trends in birth: A hospital-based cohort study. *Journal of the American Medical Association, 280,* 1849-1854.

Lang, J. M., Lieberman, E., & Cohen, A. (1996). A comparison of risk factors for labor and term small-for-gestational-age birth. *Epidemiology, 7*, 369-376.

Langer, O. (2000). Fetal macrosomia: Etiologic factors. *Clinical Obstetrics and Gynecology, 43*(2), 283-297.

Lapunzina, P., Camelo, J., Rittler, M., & Castilla, E. (2002). Risk of congenital anomalies in large for gestational age infants. *Journal of Pediatrics, 140,* 200-204.

Leishman, J. (2004). Childhood and teenage pregnancies. *Nursing Standard, 18*(33), 33-36.

Leon, D., Johannson, M., & Rasmussen, F. (2000). Gestational age and growth rate of fetal mass are inversely associated with systolic blood pressure in young adults: An epidemiologic study of 165,136 Swedish men aged 18 years. *American Journal of Epidemiology, 152,* 597-604.

Lipscomb, K. R., Gregory, K., & Shaw, K. (1995). The outcome of macrosomic infants weighing at least 4500 g: Los Angeles County and University of Southern California experience. *Obstetrics & Gynecology, 85,* 558-564.

Martin, J. A., Hamilton, B. E., Ventura, S. J., Menacker, F., & Park, M. M. (2002). Births: Final data for 2000. *National Vital Statistics Report, 50*, 1-101.

McCormick, M. C. (1985). The contribution of low birth weight to infant mortality and childhood mortality. *The New England Journal of Medicine, 312,* 82-90.

Meeuwisse, G., & Olausson, P. O. (1998). Increased birth weights in the Nordic countries: A growing proportion of neonates weigh more than four kilos. *Lakartidningen, 95*(48), 5488-5492.

Michels, K. B., Trichopoulos, D., Robins, J. M., Rosner, B. A., Manson, J. E., Hunter, D. J., et al. (1996). Birthweight as a risk factor for breast cancer. *Lancet, 348,* 1542-1546.

Mocanu, E., Greene, R. Byrne, M., & Turner, M. (2000). Obstetric and neonatal outcome of babies weighing more than 4.5 kg: An analysis by parity. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 92,* 229-233.

Mokdad, A. H., Serdula, M. K., Dietz, W. H., Bowman, B. A., Marks, J. S., Koplan, J. P. (2000). The continuing epidemic of obesity in the United States. *Journal of the American Medical Association, 284*(13), 1650-1651.

Mondestin, M. A., Ananth, C. V., Smulian, J. C., & Vintzileos, A. M. (2002). Birth weight and fetal death in the United States: The effect of maternal diabetes during pregnancy. *American Journal of Obstetrics and Gynecology, 187*(4), 922-926.

Mulik, V., Kiran, U., Bethal, J., & Bhal, P. S. (2002). The outcome of macrosomic fetuses in a low risk primigravid population. *International Journal of Gynecology and Obstetrics, 80,* 15-22.

Munroe, M., Shah, C. P., Badgley, R., & Bain, H. W. (1984). Birth weight, length, head circumference, and bilirubin level in Indian newborns in the Sioux Lookout Zone, Northwestern Ontario. *Canadian Medical Association Journal, 131,* 453-456.

Okun, N., Verma, A., Mitchell, F., & Flowerdew, G. (1997). Relative importance of maternal constitutional factors and glucose intolerance of pregnancy in the development of newborn macrosomia. *The Journal of Maternal-Fetal Medicine, 6,* 285-290.

Oral, E., Cagdas, A., Gezer, A., Kaleli, S., Aydinli, K., & Ocer, F. (2001). Perinatal and maternal outcomes of fetal macrosomia. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 99,* 167-171.

Orskou, J., Henriksen, T. B., Kesmodel, U., & Secher, N. J. (2003). Maternal characteristics and lifestyle factors and the risk of delivering high birth weight infants. *Obstetrics and Gynecology, 102,* 115-120.

Orskou, J., Kesmodel, U., Henriksen, T., & Secher, N. (2001). An increasing proportion of infants weigh more than 4,000 g at birth. *Acta Obstetrics and Gynecology Scandinavia, 80,* 931-936.

Parretti, E., Mecacci, F., Papini, M., Cioni, R., Carignani, L., & Mignosa, M., et al. (2001). Third-trimester maternal glucose levels from diurnal profiles in nondiabetic pregnancies. *Diabetes Care, 24*(8), 1319-1323.

Pettitt, D. J., & Knowler, W. C. (1998). Long-term effects of the intrauterine environment, birth weight, and breast-feeding in Pima Indians. *Diabetes Care, 21*(Suppl. 2), B138-B141.

Power, C. (1994). National trends in birth weight: implications for future adult disease. *British Medical Journal, 308,* 1270-1271.

Raio, L., Ghezzi, F., Di Naro, E., Buttarelli, M., Franchi, M., Durig, P., et al. (2003). Perinatal outcome of fetuses with a birth weight greater than 4500 g: An analysis of 3356 cases. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 109,* 160-165.

Reutter, L. (2001). Health and wellness. In P. Potter & A. Perry (Eds.; J. Ross-Kerr & M. Wood, Canadian Eds.), *Canadian fundamentals of nursing* (2nd ed., pp. 1-20). Toronto, ON: Mosby.

Rodrigues, S., Robinson, E., Kramer, M., & Gray-Donald, K. (2000). High rates of infant macrosomia: A comparison of a Canadian Native and a non-Native population. *Journal of Nutrition, 130,* 806-812.

Rodrigues, T., Teles, T. P., & Barros, H. (1999). Risk factors for macrosomia in infants of non-diabetic women. *Arquivos De Medicina, 13*(Suppl. 5), 20-23.

Rooth, G. (2003). Increase in birthweight: A unique biological event and an obstetrical problem. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 106,* 86-87.

Schaefer-Graf, U., Rossi, R., Buhrer, C., Siebert, G., Kjos, S., Dudenhausen, J., et al. (2002). Rate and risk factors of hypoglycemia in large-for-gestational-age newborn infants of nondiabetic mothers. *American Journal of Obstetrics and Gynecology, 187,* 913-917.

Silverman, B. L., Rizzo, T., Green, O. C., Cho, H., Winter, R. J., Ogata, E. S., et al. (1991). Long-term prospective evaluation of offspring of diabetic mothers. *Diabetes, 40*(Suppl. 2), 121-125.

Spellacy, W., Miller, S., Winegar, A., & Peterson, P. (1985). Macrosomia: Maternal characteristics and infant complications. *Obstetrics & Gynecology, 66,* 158-161.

Stewart, M., Gillis, A., Brosky, G., Johnston, G., Kirkland, S., Leigh, G., et al. (1996). Smoking cessation among disadvantaged women: Causes and cessation. *Canadian Journal of Nursing Research, 28*(1), 41-60.

Stotland, N. E., Caughey, A. B., Breed, E. M., & Escobar, G. J. (2004). Risk factors and obstetric complications associated with macrosomia. *International Journal of Gynaecology & Obstetrics, 87*(3), 220-226.

Surkan, P., Hsieh, C., Johansson, A., Dickman, P., & Cnattingius, S. (2004). Reasons for increasing trends in large for gestational age births. *Obstetrics & Gynecology, 104,* 720-726.

Surkan, P., Hsieh, C., Johansson, A., Dickman, P., & Cnattingius, S. (2005). In reply to a letter to the editor: Reasons for increasing trends in large for gestational age births. *The American College of Obstetricians and Gynecologists, 105*(2), 444-445.

Thomson, M. (1990). Heavy birthweight in Native Indians of British Columbia. *Canadian Journal of Public Health, 81*(6), 443-446.

Tibblin, G., Eriksson, M., Cnattingius, S., & Ekborn, A. (1995). High birthweight as a predictor of prostate cancer risk. *Epidemiology, 6*(4), 423-424.

Walter, S. D. (1980). Prevention for multifactorial diseases. *American Journal of Epidemiology, 112,* 409-416.

Wen, S. (2003). Fetal and infant health outcomes: Large for gestational age rate. In *Canadian Perinatal Health Report.* Ottawa, ON: Minister of Public Works and Government Services Canada.

Wen, S., Kramer, M. S., Platt, R., Demissie, K., Joseph, K. S., Liu, S., et al. (2003). Secular trends of fetal growth in Canada, 1981 to 1997. *Paediatric and Perinatal Epidemiology, 17,* 347-354.

Whitaker, R., & Dietz, W. (1998). Role of the prenatal environment in the development of obesity. *Journal of Pediatrics, 132*(5), 768-776.

White, D. E. (2004). *Direct and indirect determinants of low birth weight in a large Canadian urban health region.* Unpublished doctoral dissertation, University of Alberta, Edmonton, AB.

World Health Organization. (1996). Anthropometric reference data for international use: Recommendations from a WHO expert committee. *American Journal of Clinical Nutrition, 64,* 650-658.

Xiong, X., Demianczuk, N., Buckens, P., & Duncan Saunders, L. (2000). Association of preeclampsia with high birth weight for age. *American Journal of Obstetrics and Gynecology*, *183*(1), 148-155.

Xiong, X., Demianczuk, N. N., Duncan Saunders, L., Wang, F., Fraser, W. D. (2002). Impact of preeclampsia and gestational hypertension on birth weight by gestational age. *American Journal of Epidemiology*, *155*(3), 203-209.

Xiong, X., Mayes, D., Demianczuk, N., Olson, D. M., Davidge, S., Newburn-Cook, C., et al. (1999). Impact of pregnancy-induced hypertension on fetal growth. *American Journal of Obstetrics and Gynecology*, *180*(1), 207-213.

Yeazel, M. W., Ross, J. A., Buckley, J. D., Woods, W. G., Ruccione, K., & Robison, L. L. (1998). High birth weight and risk of specific childhood cancers: A report from the Children's Cancer Group. *Journal of Pediatrics, 131*(5), 671-677.

Yeh, J., & Shelton, J. (2005). Letter to the editor: Reasons for increasing trends in large for gestational age births. *The American College of Obstetricians and Gynecologists*, *105*(2), 444.